

THE PRACTITIONER

No. 961

JULY 1948

Volume 161

THEN AND NOW

By SIR HENEAGE OGILVIE, K.B.E., M.D., M.Ch., F.R.C.S.

The Practitioner was founded eighty years ago by Dr. Anstie of the Westminster Hospital, the first number appearing in July 1868. The *Lancet*, at that time a combative and even aggressive journal, was the senior and most influential of the medical periodicals. July 1868 was an excessively hot month, and the *Lancet* discussed measures that should be adopted to ward off the sun's rays, advocating the wearing of white flannels; advice that was commented on in *Punch*.

The pages of *Punch* for 1868 give a very fair picture of the England into which our journal was born. They reveal a country settled and secure, concerned above all with its own affairs, with the personalities rather than with the policies of its leaders, with the minutiae of social adjustment rather than the struggles of classes or the rivalries of nations. The chief concern of Parliament in that important month was whether or not the half-crown, which had not been issued for fifteen years, should be withdrawn from circulation. Gladstone and Disraeli were in their prime. The conservatives were in office in July, but their hold on the country was clearly waning, and in a general election in the autumn the liberals scored a sweeping victory. The chief matter under dispute was the disestablishment of the Irish Church. Foreign politics received only passing consideration, and then merely as they affected the prestige and dignity of England. Napier's successful expedition to Abyssinia, to liberate certain British subjects held in captivity by the Emperor Theodore, had caused a very general satisfaction, but the cost of the campaign had forced the income tax up to 6d. in the pound. France was viewed with a certain amount of hostility as a possible aggressor, but Germany was seldom mentioned, and no hint appeared of the tension which was to flare up two years later in the Franco-Prussian war. The jokes were almost all concerned with the minor awkwardnesses and major disasters of a nicely graded social system, in which everyone knew his place and intercourse was conducted according to ordained and carefully served rules and procedure. Languid Johnnies in whiskers and gracious young ladies, with their foils, the bouncer and the adventuress, were the chief actors. Bathing in this phenomenally hot summer was still conducted with the utmost decorum. The sexes undressed and donned their full-length bathing costumes in separate bathing machines which were then backed into the sea, when a folding canvas hood was let down over the steps, so that

based on the results of statistical inquiry, not into single cases, but into thousands compared and classified. Pharmacy, relying on the medicinal properties of crude drugs of vegetable or mineral origin, has given way to chemotherapy by pure substances refined by extraction or prepared by synthesis, each selected for a particular action on the body or its enemies, and blue-printed to exercise that particular effect.

It is a commonplace that scientific discovery, proceeding ever at greater speed, has transformed all political issues. A nation that does not use science, both for research and production, will soon be unable to feed, much less to defend, itself, for it will neither be able to compete in the world's markets nor give its people the standards of life they demand. It may be predicted that even an iron curtain will not always hide from any people their own relative hardship compared with those who are more advanced. And medicine, which has always demanded some degree of centralized control, has more to gain even than industry from organization designed to subsidize clinical and laboratory research.

Organization must come, in all states and in all sciences. The situation must be accepted; but in that situation, as in all political situations, there are great dangers as well as great opportunities. Organization is no substitute for genius. No amount of bureaucracy could have discovered penicillin. But once the indispensable man of insight has perceived a crack in the wall of ignorance it does not require a genius, but only weight and size, to knock a hole in it. States can provide the mass attack, and in the future it will be their business to do so; but they must beware lest the essential genius of discovery, which will always be individual and unpredictable, be overlaid among committees and strangled by red tape. Red tape is essential to organization. It is as much a part of a state scheme as the rigging of a ship, which holds up the masts. We must see to it that the rigging is limited to that which is needed to provide an efficient sail plan; that it is as light as correct design and modern materials will allow; that it does not set up windage and hinder progress. We must see to it that the ship itself is on the right course and under the right direction.

Bureaucracy, by its very nature, tends to go beyond its mandate. Its job is to regulate, and it is thus apt to love regulation for its own sake, to look on rules as the end rather than the means of administration. There is the constant danger that it may rule out discovery itself. As a bureaucracy kills with its rules, so a committee may crush with its dogmatism. All committees run to dogma, largely because they consist of several persons obliged to agree on one decision. These persons, if they have any opinion at all, must differ in some part of the matter, and commonly agreement can be found only in what is called a broad ruling, that is, a lowest common denominator founded on some idea derived, not from individual experience, but from an instruction in which all have been brought up—that is, a dogma. And since authoritative committees usually consist of persons of mature age, these dogmas are often out of date.

only the ankles of the entering bather could be seen by the curious as he or she entered the water. In 1868 London was visited by the Scotsman who complained that he had not been there two hours when "bang went saxepe".

Since *The Practitioner* was founded a third political party has emerged, grown, and finally wrested power from the two older ones that had held alternate sway since the time of the civil wars, and had fought for dominance in 1868. There have been five major wars, in three of which Britain has played a major part. The backward races of the last century have emerged to self-conscious nationalism. America has assumed the financial domination of the world. Transport has been revolutionized; first came the bicycle, which by its abolition of group conventions and parental discipline has been one of the most potent forces in moulding the social structure of the age; then the internal combustion engine bringing the motor car, the fast ship and the aeroplane, which between them have homogenized nations and are on their way to suburbanize the world.

The contrast between the medicine of eighty years ago and that of to-day, is possibly even greater. Dr. Bett's analysis of the first volume of *The Practitioner* reveals a state of affairs in which the science of clinical observation stood high, but that of pathology was confined to what is now known as morbid anatomy. Little was known of the causation of disease, and in therapeutics blood-letting and the poly-pharmacy of the alchemist still persisted. Since that day the science of bacteriology has appeared, and the control of sepsis has enabled surgery to take over the treatment of many diseases. The recognition of parasitic, bacterial and virus infections; of allergy; of the part played by the endocrine system in health and disease; of nutritional deficiencies due to lack of basic foodstuffs of the accessory food factors or of individual organic and mineral constituents; of the action of endogenous and exogenous toxins; and of the part played by the mind in sickness and in health; all these have laid the basis of a scientific or at any rate of a reasoned classification. Precision methods of many kinds have made diagnosis more exact. The increasing field of operative treatment has led to the subdivision of surgery into a group of specialisms, the number of which is still increasing. Radiology and radiotherapeutics have appeared. Anæsthesia has become a skilled science. Social legislation, much of which has been medical or had medical implications, has virtually abolished the major epidemic scourges and those diseases which had their origin in overcrowding, unhealthy trades, malnutrition, and lack of sanitation.

In general, the most profound change for the world in the last eighty years has been in the progress of science, not alone in its methods, but in its reach. The reach of science has extended in both directions; in the precisior of minute analysis, and in the application of discovery. Factories are now organized on a scientific basis; each has its research department, and the laboratory investigations of to-day are the basis of the full-scale production of to-morrow. Clinical medicine is no longer a matter of impressions, but is

THE MODERN CONCEPT OF SOCIAL MEDICINE

By JOHN A. RYLE, M.D., F.R.C.P.

Professor of Social Medicine in the University of Oxford.

TEN years, even six or seven years, ago the term "social medicine" was not often used. Now, in Great Britain and Northern Ireland, there are four Institutes and Chairs of Social Medicine and, in addition, others connected with Industrial Health and Child Health which have many comparable objectives and must shortly extend their interest to a fuller consideration of social influences as these affect working populations and the earlier age-groups. A special committee of the Royal College of Physicians (1943) and the Goodenough Committee (1944) urged the importance of developing teaching in social medicine in all the medical schools. As long ago as 1936 the General Medical Council recommended that "throughout the whole period of study the attention of the student should be directed by his teachers (a) to the importance of measures by which normal health may be assessed and maintained, and (b) to the principles and practice of the prevention of disease". René Sand in Belgium was, I believe, the earliest European pioneer in the new educational trend. His recently published "*Vers la Médecine Sociale*" is a valuable historical study of the subject. Cabot and Canby Robinson in the United States were also early advocates of reform. Sir Arthur MacNalty, Sir Wilson Jameson, and Professor Major Greenwood in England have for long sponsored the wider acceptance of the principles of modern socio-medical philosophy and practice. New types of collaborative research—employing physicians, statisticians, medical social workers and others—are in the course of development. At the recent International Conference of Physicians in London (1947), two days were devoted to the discussion of matters of socio-medical interest, including the place of social medicine in the curriculum, social surveys in relation to medicine and psychiatry, and the care of the aged. In many other countries there is a resurgence of interest in the subject. Inevitably it will be necessary to pass through a period of readjustment—a transitional and experimental period—but that the ideas of social medicine and its related sciences of social pathology and hygiology are likely, in due course, to influence profoundly the whole discipline and practice of Medicine can scarcely now be disputed.

As to the reasons for this ferment of interest, I would suggest that it has been prompted partly in concert with our present transition, as Julian Huxley has described it, from the age of "economic" to the age of "social" man, an age of increased social thinking and planning; but partly also in response to many current dissatisfactions born of over-specialization and the

We must remember, too, that the innovators and geniuses of this generation are likely to become the doctrinaires of the next. For science moves, and none can predict the direction of its movement; and in the tide of scientific change the problems of control are more those of the navigator who explores perilous seas, than of the lawyer who drafts a bill or the dictator who imposes a regime.

The National Health Service Act has now been accepted by Parliament and is on the statute book. No liberal profession can accept the prospect of regimentation with anything but distaste, and doctors, with their peculiarly personal relationship to their patients, cannot help viewing the threat of nationalization, and the suppression of individual liberty that this implies, with repugnance. The Minister has given his assurance that a whole-time nationalized service is not intended; his concessions may not go as far as the majority would wish, but they show a willingness to meet the objections of the profession that speaks well for the future. We, as loyal members of a democracy, must see that the citizens of the country do not suffer even while, as a profession, we strive to correct the crudities of the service as it is presented to us.

The practical difficulties facing the scheme at its outset are great. On July 5, nearly every man and woman in the country will be asked to pay full contributions for promised benefits, very few of which are available or will be available for many years to come. Had the Government been prepared to content themselves for the time being with that part of the programme which could be implemented, the unification of the Hospital system, they would have had the practically unanimous support of the profession. Further, they would have had some prospect of making a success of it, and, in ten years or so, with this success behind them, they could have introduced a unified scheme of domiciliary practice.

The ultimate success of the scheme will depend almost entirely upon our cooperation, and for the sake of the country and of the sick and suffering we must do what we can to make a success of what we cannot but regard as hastily prepared and unpromising material. In the negotiations that preceded the introduction of the Act we made it clear that we did not consider the scheme in its present form to be a sound one, and we could not therefore accept responsibility for the inevitable failings that would appear as soon as it was introduced. Now it is in being, we must strive with all our might to ensure that our patients continue to receive the service we have always given them in the past.

Difficult times lie ahead; but difficult times have always produced great leaders. Let us pray that the medical profession will itself bring forth such leaders and that, in spite of all difficulties, they will succeed in building a successful service, one in which we can work to the benefit of our patients, one in which we may be proud to play a part.

SOCIAL MEDICINE AND PUBLIC HEALTH

But if the philosophy and the discipline now under review have, as has been suggested, their applications to all branches of medical thought and practice in their bearing upon the individual and his family, the very names "social medicine", "social pathology" and "social hygiology" imply a special concentration of interest upon larger groups, societies or populations. In this regard the epidemiology, etiology and prevention of community disease and the etiology and promotion of community health become their chief concern. It is thus proper to ask what distinctions are to be drawn between the earlier concept of public health and the modern concept of social medicine. Which is the more suitable and comprehensive term? The following would seem to be the main distinctions:—

(1) In public health, for evident reasons and for a long time, emphasis was placed on the *environment*. Bad environments were a main cause of disease and called urgently for improvement. Social medicine places the emphasis on *man* considered in relation to his environment. Here, too, it extends the idea of environment to include the economic, nutritional, domestic, occupational, educational and psychological experience or opportunity of human communities. The modern public health worker recognizes that these are to-day susceptible of more intimate study and even sometimes of measurement by a combination of the accepted procedures of social, medical and statistical research, and, furthermore, of modification by methods outside the scope of earlier sanitary practice.

(2) Public health for a long time, and again for very good reasons, was chiefly concerned with the *communicable diseases*. Social medicine is concerned with *all diseases of prevalence*, including, for example, rheumatic heart disease, peptic ulcer, cancer, the chronic rheumatic diseases, appendicitis, the neuroses and accidental injuries; all of which have their etiologies in some measure linked with social factors and all of which can be thought of ultimately as being in greater or less degree preventable.

(3) Social medicine, or, perhaps, it should here be referred to as social hygiene, has an intimate concern for constructive policies directed to the improvement of health (as distinct from the prevention of disease) by nutritional, educational and recreational methods. In modern public health practice the midwife and the health visitor, the maternity and child welfare centres and school services, and the health education programmes of the local authority and other agencies have here made increasing contributions to the advancement of the practice of social medicine.

(4) Where hospital practice (as distinct from protective or constructive practice) is concerned, social medicine further takes within its ambit the special work of the hospital or municipal almoner as medical social worker. Social diagnosis and therapeutics, pursued in parallel with the medical inquiries and ministrations of the institution or clinic, and having as their final objective a more complete assistance to, and a more final restoration of, individuals and families for effective work and living after illness, are her principal tasks. In her case, as in that of the practitioner, the focus of interest is upon the patient and his family, whereas that of the health authority is upon the community as a whole. But the principle of consideration for *total circumstance* and for a *continuing extension of health opportunity* should be accepted by every branch of the service.

Briefly, then, it may be said that "social medicine" extends the interest and redistributes the emphasis of the older "public health". Similarly, "social pathology" extends the interest, broadens the emphasis and advances the techniques of the older "epidemiology". There is thus nothing implicit in the modern concept of social medicine which can be considered as conflicting with the work or motives of the public health services. For

dominance of technological over humanistic methods of instruction and study. It is also at last being realized how, as a consequence of preoccupation with disease, the associate problems of health and its etiology, its measurement, its promotion and its maintenance, have been neglected. In the search for specific causes, whether presenting themselves as bacterial invasion or nutritional defect, it is now realised that far too little thought has been given to the social conditions without which these agencies must fail to find their opportunity.

DEFINITIONS

How should social medicine be defined? I would ask, in the first instance, that it be considered not only as something that can be practised and as capable of exerting its influence through every branch of professional thought and activity—constructive, preventive, and remedial—but also as *a scientific discipline* essential to a sound medical and social philosophy and to the advancement both of knowledge and of practice. Not dissimilarly, although it has been allowed to concentrate unduly upon present sickness and immediate service for the detached individual, has clinical medicine been considered on the one hand as a form of practice, and on the other as an academic discipline directed to the improvement of knowledge and of professional standards. Although at present the development and extension of its ideas and methods have attracted to it special attention, it would be wholly incorrect to think of social medicine as a new kind of specialism. If human physiology and pathology are accepted as among the more important related sciences of clinical (or individual) medicine, so now should *social hygiology* and *pathology* (studied collaboratively by the methods of the physician, the statist, the medical social worker, the radiologist, the nutritional physiologist, the field epidemiologist, and others) be accepted as the main related sciences of social medicine.

It cannot be too strongly insisted that the disciplines of the ward as well as those of protective and constructive medicine have need to adopt and absorb the lessons of modern socio-medical teaching. Every diagnosis has its social as well as its personal and pathological component, and the treatment, especially of chronic conditions, commonly requires the assistance of careful and expert social inquiry, and of adjustments of work and living conditions. A perfect arthrodesis for a tuberculous knee joint (a condition often traceable to influences which might have been prevented from becoming operative) has a limited value if the patient, on leaving hospital, has to live in a squalid room on an inadequate income, and with no good prospect of obtaining suitable work. It is a remarkable thing to see an infant with tuberculous meningitis recovering under streptomycin; but it would have been better if its aunt, resident in the house and a victim of open pulmonary disease, had been found alternative accommodation so that infection could have been avoided. Social diagnosis and social therapeutics must more frequently serve to complete institutional assessment and treatment, and to rationalize the instruction of the student.

tional studies of human communities at risk could more often have assisted or even anticipated the work of the dead-house and the laboratories. Whereas there was failure at first to deal with lead and phosphorus and silicosis hazards, there should now be success from the beginning in protective actions against the hazards to which scientists and technicians will be exposed in the course of atomic research and its applications. Whereas it has been necessary to wait for the nutritional physiologist to confirm, extend and refine the early observations of Captain Cook, of Glisson and of Trousseau, and to reveal the special effects of patently inadequate diets, in future, with the aid of socio-medical and other survey work, it should be possible to plan both for a better quality and quantity of food and for its more equitable distribution in the world. In all these matters medical men bear a large part of the responsibility and need the mental orientation necessary to its wider fulfilment.

The *research developments* of social pathology and hygiology will be based upon our new university institutes of social and industrial medicine and child health, or sponsored by the Medical Research Council, the London School of Hygiene, or other bodies. Employing clinical, statistical and sociological methods and techniques in varying combination these departments will have ample problems to engage them for generations to come. Hygiological studies conducted upon ostensibly healthy populations will also fall to the school medical officer, physicians in charge of student health services, and the medical and scientific officers of the armed forces.

In *teaching*, the hospital physician and surgeon will need to think more constantly in terms of *patients* and their circumstances and less in terms of *cases*. Their beds provide ample texts in social medicine. They should encourage their clerks and dressers to include systematic social histories in their reports, supplemented and amplified when necessary by the more detailed and expert report of the almoner. Lectures on social medicine and hygiene and classes in the elements of medical statistics will need to be related more closely to clinical teaching and should be distributed over at least one clinical year. Socio-medical case-conferences, field visits to the factory, the slum and the new housing estate should be brought within the programme. At least fifty hours out of the six years' training should be specifically devoted to the course. These hours (as has been shown at Oxford) can be found and should surely to-day be regarded as *a necessary part of general medical training*. If need be, hours should be abstracted from more highly specialized teaching, much of which, in any event, would be better deferred to the postgraduate phase. When every medical school has its related practitioner unit working in a neighbouring health centre, short periods of apprenticeship in family practice should become a statutory part of the medical student's training, whether before or soon after graduation. Physical standards and their assessment, normal variability in structure and function, and the influence of nutrition on growth and health, might well receive a fuller emphasis in the departments of anatomy and physiology.

these too, it is true, there is need to consider a revision of programmes and a broadening of sociological and epidemiological interest, but, by the steady extension of their work from environmental improvements to the personal services, they have already given practical demonstrations of that shift of emphasis from the environment to the living community already referred to. All accept to-day that more and better homes, a national food policy, school meals and school milk, and further industrial health supervision and legislation are, or should be, among the tangible expressions of the practice of social medicine in its national setting. It is agreed that these things have, in fact, a far greater contribution to make to the popular health than have all the hospitals and all the remarkable new chemotherapies and surgical technologies put together. New research and reformed teaching, and an ever-increasing permeation of the professional, legislative and popular mind with the ideas and principles of social medicine, are what are now required.

CHANGING DISCIPLINES

What reforms in research and teaching should be envisaged? The development of collaborative survey methods involving the physician, the statist, the medical officer of health, the industrial medical officer, the social worker, and others, and their application to the study of different populations or population samples (whether determined by age, sex, occupation or geography) has already made, and will continue to make, important contributions. Community diagnosis must supplement individual diagnosis. Official mortality studies will need to be largely supplemented by morbidity studies. The epidemiology and etiology of cancer, peptic ulcer, appendicitis, coronary disease, rheumatic heart disease, the psychoneuroses, and the countless accidental injuries which crowd our hospitals, must be studied both in old and in new ways. With the declining fertility and increasing expectation of life which obtain in most Western communities to-day, we are faced with ageing populations. Old age presents increasing problems. There is an increase of sickness of certain kinds in early adult and middle life, due in part to the multiple stresses which accompany the speed and competitive strife of the modern world. But a much greater saving of life in infancy and childhood is still possible. In India, Asia and Africa, and in our Colonial dependencies, on the other hand, the major problems are still those of high fertility and a low expectation of life; of poverty, squalor, insanitary surroundings, poor nutrition, and illiteracy.

It will be among the particular functions of social medicine and its related sciences *to anticipate the effects of social change*. In the past, too often have the consequences of such adverse factors as nutritional defect and occupational hazard been left undealt with until they had already claimed innumerable victims. Such delays should not in future be inevitable. Scientific research has repeatedly supplied the necessary knowledge and impetus for action, but the lag period has been long, and social occupa-

tional studies of human communities at risk could more often have assisted or even anticipated the work of the dead-house and the laboratories. Whereas there was failure at first to deal with lead and phosphorus and silicosis hazards, there should now be success from the beginning in protective actions against the hazards to which scientists and technicians will be exposed in the course of atomic research and its applications. Whereas it has been necessary to wait for the nutritional physiologist to confirm, extend and refine the early observations of Captain Cook, of Glisson and of Trousseau, and to reveal the special effects of patently inadequate diets, in future, with the aid of socio-medical and other survey work, it should be possible to plan both for a better quality and quantity of food and for its more equitable distribution in the world. In all these matters medical men bear a large part of the responsibility and need the mental orientation necessary to its wider fulfilment.

The *research developments* of social pathology and hygiology will be based upon our new university institutes of social and industrial medicine and child health, or sponsored by the Medical Research Council, the London School of Hygiene, or other bodies. Employing clinical, statistical and sociological methods and techniques in varying combination these departments will have ample problems to engage them for generations to come. Hygiological studies conducted upon ostensibly healthy populations will also fall to the school medical officer, physicians in charge of student health services, and the medical and scientific officers of the armed forces.

In *teaching*, the hospital physician and surgeon will need to think more constantly in terms of *patients* and their circumstances and less in terms of *cases*. Their beds provide ample texts in social medicine. They should encourage their clerks and dressers to include systematic social histories in their reports, supplemented and amplified when necessary by the more detailed and expert report of the almoner. Lectures on social medicine and hygiene and classes in the elements of medical statistics will need to be related more closely to clinical teaching and should be distributed over at least one clinical year. Socio-medical case-conferences, field visits to the factory, the slum and the new housing estate should be brought within the programme. At least fifty hours out of the six years' training should be specifically devoted to the course. These hours (as has been shown at Oxford) can be found and should surely to-day be regarded as *a necessary part of general medical training*. If need be, hours should be abstracted from more highly specialized teaching, much of which, in any event, would be better deferred to the postgraduate phase. When every medical school has its related practitioner unit working in a neighbouring health centre, short periods of apprenticeship in family practice should become a statutory part of the medical student's training, whether before or soon after graduation. Physical standards and their assessment, normal variability in structure and function, and the influence of nutrition on growth and health, might well receive a fuller emphasis in the departments of anatomy and physiology.

these too, it is true, there is need to consider a revision of programmes and a broadening of sociological and epidemiological interest, but, by the steady extension of their work from environmental improvements to the personal services, they have already given practical demonstrations of that shift of emphasis from the environment to the living community already referred to. All accept to-day that more and better homes, a national food policy, school meals and school milk, and further industrial health supervision and legislation are, or should be, among the tangible expressions of the practice of social medicine in its national setting. It is agreed that these things have, in fact, a far greater contribution to make to the popular health than have all the hospitals and all the remarkable new chemotherapies and surgical technologies put together. New research and reformed teaching, and an ever-increasing permeation of the professional, legislative and popular mind with the ideas and principles of social medicine, are what are now required.

CHANGING DISCIPLINES

What reforms in research and teaching should be envisaged? The development of collaborative survey methods involving the physician, the statist, the medical officer of health, the industrial medical officer, the social worker, and others, and their application to the study of different populations or population samples (whether determined by age, sex, occupation or geography) has already made, and will continue to make, important contributions. Community diagnosis must supplement individual diagnosis. Official mortality studies will need to be largely supplemented by morbidity studies. The epidemiology and etiology of cancer, peptic ulcer, appendicitis, coronary disease, rheumatic heart disease, the psychoneuroses, and the countless accidental injuries which crowd our hospitals, must be studied both in old and in new ways. With the declining fertility and increasing expectation of life which obtain in most Western communities to-day, we are faced with ageing populations. Old age presents increasing problems. There is an increase of sickness of certain kinds in early adult and middle life, due in part to the multiple stresses which accompany the speed and competitive strife of the modern world. But a much greater saving of life in infancy and childhood is still possible. In India, Asia and Africa, and in our Colonial dependencies, on the other hand, the major problems are still those of high fertility and a low expectation of life; of poverty, squalor, insanitary surroundings, poor nutrition, and illiteracy.

It will be among the particular functions of social medicine and its related sciences *to anticipate the effects of social change*. In the past, too often have the consequences of such adverse factors as nutritional defect and occupational hazard been left undealt with until they had already claimed innumerable victims. Such delays should not in future be inevitable. Scientific research has repeatedly supplied the necessary knowledge and impetus for action, but the lag period has been long, and social occupa-

THE NATIONAL HEALTH SERVICE ACT

By A. LESLIE BANKS, M.D., F.R.C.P., D.P.H., *Barrister-at-Law.*

Principal Medical Officer, Ministry of Health.

It was in 1854, fourteen years before the foundation of *The Practitioner*, that Sir John Simon wrote his essay on a Ministry of Health. This essay, written as a preface to the volume of the reprinted City of London Reports, did more than anticipate the formation of the Ministry of Health in 1919. It visualized "comprehensive and scientific legislation" whereby a department would be created with a constituted head, sitting in Parliament, responsible in the widest sense "to care for the physical necessities of human life . . . the people, through its representatives, must be able to arraign him wherever human life is insufficiently cared for".

On July 5, 1948, there will come into force legislation whereby this dream of Sir John Simon will be realized. But a nationally organized medical service regulated by a written code is not a new thing. In Babylon, some time between 1948 and 1905 B.C., King Hammurabi was engaged on a similar task. His code was placed in the market places and fragments still survive. It is clear from the medical portions still available that it was a brutal code, no doubt suited to the needs of the time, but it does show definite State intervention in the organization of medicine. Take this example:—

"If a doctor shall treat a gentleman and shall open an abscess with a bronze knife and shall preserve the eye of the patient, he shall receive 10 shekels of silver. If the patient is a slave, his master shall pay two shekels of silver".

Next comes what we should now term a penal clause:—

"If a doctor shall open an abscess with a bronze knife and shall kill the patient or destroy the sight of the eye, his hands shall be cut off".

If a slave died, the doctor had to replace the slave with another.

The Babylonian civilization passed, but traces of the ancient code of "an eye for an eye, and a tooth for a tooth" persisted.

Each civilization in turn has produced evidence of an organized medical service and each has bequeathed something to its successors. Egypt gave us the Ebers Papyrus and the symbol of the eye of Horus placed on such dangerous objects as ships and chariots and to-day reserved for medical prescriptions. The Mosaic code with its emphasis on the fundamental principles of hygiene; the beautiful clinical records, high standards of medical practice and natural therapy of the Ancient Greeks; the State hospitals and teaching of the Roman Empire, all reveal evidence of organized care for the health of the community. Indeed, Martial's epigram might well be

Improved teaching will need to be reflected in more rational examination papers—in those relating to general medicine, surgery, pædiatrics and obstetrics, as well as in those directly concerned with public health doctrine.

CHANGING PRACTICE

In the coming years the general practitioner will have his intimate part to play, as did the country doctor of the past. In cities and towns especially he should have a far better opportunity of practising social medicine than ever before when he works as a member of a team and in closer cooperation with others, whether of the social and public health or hospital services, and with a well-staffed and equipped health centre as his base of operations. The consultant and specialist, as members of a comprehensive service, should also be able to play a fuller part as their cooperation with the other services of a region improves, and as they learn the value of the assistance which the almoner (freed from clerical duties and monetary assessments) can give. The medical officer of health will have new opportunities for the development and re-direction of his epidemiological interests and for the closer coordination of sanitary, remedial and social services. His use and status as a consultant call for much wider recognition. Periodic group consultations between representatives of the public health, practitioner and consultant services of a city or region could come to have great value.

SUMMARY

The health and sickness of the people are, in brief, overdue for study by other methods than the high-power microscope of ward and laboratory research. The health of the people which has, in theory, been accounted "the highest law", must have its own natural laws more firmly established by social and scientific studies, as thoughtfully integrated and as liberally developed as may prove possible in a socially better informed and more co-operative age. Nothing could so well renew the heart in Medicine—itsself the oldest social science and service—as a renewal and extension of interest in men, women and children; in the way they live together; in the conditions of their work; and in their economic and educational opportunities or needs. Socio-medical surveys and statistical studies—since they advance knowledge, inspire teaching, and lead to rational actions, and since their practical implementations can, for instance, be measured by such things as a decline in early mortality or morbidity, improved growth and health in children, better performance in industry and improved heights, weights and efficiency in military recruits—must be accepted as at least as valuable, both scientifically and operatively, as new discoveries in the laboratory and new advances in diagnostic or therapeutic methods. It should even become possible, in due course, to advance from the old idea of an indefinite humane art to that of a better defined and humanistic science, whose methods will be as much respected by other scientists as its contribution to their service will be respected by the common people.

because it has proceeded silently. The discovery of X-rays; the vast improvement in surgical technique during the two world wars; the growth of chemotherapy; the tremendous advances in bacteriology, and the discovery of modern insecticides such as DDT, are already part of our daily lives. Equally important are the changes within the framework of the medical profession. The great individualist of the nineteenth century is being replaced by the team. Within the memory of many men still in active practice the art of medicine has changed from purely clinical methods to a series of exact sciences.

The State has been forced by the dramatic events of the past forty years to interfere, not only by measures to protect the public health, but also in the personal health services. Until the beginning of the present century, the natural increase of the population more than compensated for the losses from ill-health and epidemic disease. The general tempo of life was much slower, and in Victorian times competition between the nations followed well-understood channels. With the turn of the century the pace of domestic life quickened, competition among the Western Nations became fierce, and losses by modern methods of war very great. At the same time, the natural fertility of the people began to decline. It became necessary to revise all earlier notions, and to-day the picture is quite different. The public conscience has long demanded that each avoidable death should be prevented, and this demand is now reinforced by the need to maintain each member of the State in the highest degree of physical and mental fitness. The burden of expenditure on sickness under modern conditions can be a crushing one. To give only one example: the case of pulmonary tuberculosis which requires a thoracoplasty may cost £1,200 from the time the patient enters hospital for operation until his discharge some months later. Sober consideration of these facts makes it clear that some form of National Health Service had become inevitable.

THE SCOPE OF THE NEW HEALTH SERVICES

Before the National Health Service Act is considered in detail, it is necessary to glance for a few moments at other social measures with which it is linked, as a number of statutes recently passed interlock in their relationship to the health services of the country. In particular, the Education Act of 1944, the National Insurance Act and the National Health Service Act have, as a common denominator, the provision of a comprehensive medical service for the whole nation. Section 48 of the Education Act makes it the duty of every local education authority to secure comprehensive facilities for free medical treatment of school children, and this range of treatment joins inevitably with that other comprehensive service to be provided under the National Health Service Act. Even now the picture is not complete, and we shall not see the full extent of social legislation until the Act abolishing the Poor Law and establishing a system of national assistance is implemented.

applied in our present-day teaching hospitals:—

“I’m ill. I send for Symmachus. He is here.
A hundred students following in the rear.
All paw my chest, with hands as cold as snow,
I had no fever, but I have it now”.

The slow development of medicine in Western Europe provides a fascinating study. The early Christian preoccupation with the affairs of the spirit retarded development until Tudor times. To Henry VIII, for his Charter to the Royal College of Physicians and recognition of the union of the surgeons, and to his daughter Elizabeth, for the foundation of the Poor Law, may be ascribed the beginning of our present services. The scientific advances in the reign of Charles II, and the setting up of the voluntary dispensary and hospital system in the eighteenth century, paved the way for the tremendous advances in clinical medicine and pathology in the nineteenth century.

The turn of the 20th century saw a somewhat *laissez-faire* England and a medical profession which appeared to have reached the peak of clinical knowledge. The next forty years were to see this picture completely changed. There are many factors to account for this but they may be divided broadly into three interrelated groups. First, there was the occurrence of three great wars; next, the growth of State intervention in medicine, and, lastly, remarkable discoveries in medical and allied sciences.

THE GROWTH OF STATE MEDICAL SERVICES

The Boer War shook Victorian England to its foundations. Apart from the startling fact that a little nation could defy the British Empire for so long, there was the realization that numbers of recruits for the army were physically unfit to serve. This low physical standard coupled with the growth of large continental armies made early action by the State imperative. A Royal Commission set up to investigate the matter resulted in the formation of the School Medical Service in 1907. Once started, the interest of the State continued. Attention was next directed to maternal and child welfare. 1911 saw the first National Health Insurance Act. Almost before these measures could take effect came the first world war, and the effect of the carnage of 1914 to 1918 was to intensify State intervention in the care of the people’s health. Examples may be given of the V.D. Regulations, 1916; Maternity and Child Welfare Act of 1918; and the formation of the Ministry of Health in 1919. The mass of health legislation from 1918 onwards is well known, and it is only necessary to mention the Local Government Act of 1929 and the great consolidating Public Health Act of 1936 as examples. Then came the second world war. The effect of the struggles of 1939-45 has been to produce a social and financial revolution of which we now only dimly perceive the outlines. At the same time there has been an equally important revolution within medicine itself. This is none the less striking

and young children, health visiting, home nursing, immunization services, ambulance services, and health centres. It is necessary to look at these various sections as duties laid on the local health authority with one end in view. They make the local health authority responsible for a service for the care of the people in their homes supplementary to the clinical care provided by the general practitioners and the hospitals.

The main burden of *the mental health services* falls on the regional hospital boards which will administer both mental hospitals and mental deficiency colonies. They will also be responsible for the coordination of the specialist services for mental health throughout the region, including diagnosis, advice and treatment at child guidance clinics. The ascertainment of mental defectives and the care of defectives in the community, other than those on leave or licence from institutions, become the responsibility of the local health authority.

The main divisions of the National Health Service are, therefore:—

(1) The hospital and specialist services administered by the boards of governors of the teaching hospitals, and the regional hospital boards through the hospital management committees.

(2) The general medical, dental, pharmaceutical and supplementary ophthalmic services, administered through the local executive councils.

(3) The local health authority services consisting of the care of mothers and young children, midwives service, health visitors, home nursing, the prevention of illness, care and after-care in the home, domestic help, ambulance service and immunization against diphtheria and smallpox, administered by the county and county borough councils through their statutory health committees.

(4) Mental health service administered partly by the regional hospital boards and partly by the local health authorities.

Two questions spring immediately to mind. First, how are these various branches to be coordinated, and secondly, what part does the doctor, on whose advice and cooperation the success of the entire service depends, play in the general administration?

Coordination is ensured at three levels: the Minister of Health is answerable to Parliament for the efficiency of the whole service. This means that in addition to the searching test of parliamentary questions his department must be prepared to deal with suggestions, recommendations and complaints from all sources. Ultimate financial control of the whole service, with the exception of the local health authorities which contribute approximately 50 per cent. of the cost of their services from the rates, rests also with the Minister. The machinery of central advisory committees is also provided. In addition, the formal and informal discussions with deputations and between officers which form the bulk of the day-to-day work of the Ministry will continue. Coordination between the various bodies responsible for local administration of the service is ensured by interrepresentation on the governing bodies and committees, and by the requirement that important developments must be the subject of consultation. Liaison between the officers of the boards of governors, regional hospital

Naturally the greatest effect on hospital and health services is produced by the National Health Service Act.

This is an Act to provide for the establishment of a comprehensive health service for England and Wales and for purposes connected therewith. It is divided into six parts and ten schedules. Part 1 deals with central administration, including the formation of a Central Health Services Council to advise the Minister; Part 2 deals with hospital and specialist services; Part 3 deals with health services provided by the local health authorities, i.e., the county and county borough councils; Part 4 is concerned with general medical, dental, pharmaceutical, and supplementary ophthalmic services; Part 5 makes special provision as to mental health services.

That is the broad structure of the Act, and it is the essence of it that all the different branches dealt with under the Act are coordinated to form one service, with the Minister of Health answerable to Parliament for the whole.

The hospitals.—The local administration of hospital and specialist services falls upon Regional Hospital Boards which, in turn, delegate most of the day-to-day administration of these hospitals to hospital management committees. The regional hospital boards retain, as clearly they must, the organization of specialist services. To be effective these must be planned and coordinated over the whole region. There are 14 hospital regions, 4 of which deal with London and the Home Counties and the remaining 10 with the rest of England and Wales. Linked with each region will be the teaching hospitals, undergraduate and postgraduate, of the parent university; and the board of governors of these hospitals will work in close association with the regional hospital board, thereby ensuring that the influence of university teaching and research is spread throughout the region. The teaching hospitals will also share in the care of the acute and chronic sick of the area. Power has been taken in the Act to continue in permanent form the emergency public health laboratory service and the blood transfusion service.

The administration of the *domiciliary medical, dental and ophthalmic services* is the responsibility of specially constituted Executive Councils. The area covered by each executive council corresponds broadly with that of the county or county borough in which it is situated, but in some areas it has been found convenient to set up one executive council to deal both with the county borough and the adjoining county. It is clearly necessary to ensure that the work of the executive councils is closely linked with that of regional hospital boards, and the latter are required to consult the former before setting up the hospital management committees in any area.

Part III of the National Health Service Act deals with the duties of the new *local health authorities*. These are the county and county borough councils and upon them is laid a number of new responsibilities. At first glance it may appear that these are merely extensions of the old disconnected powers which arose out of a variety of Acts. Closer examination will show, however, that this is not the case. Sections 19-30 of Part III of the Act deal with such matters as the provision of a midwifery service, care of mothers

general practitioner has never acquired the North American habit of going to an "office". The section of the Act relating to health centres lays down that they shall provide accommodation for general medical and dental practice in addition to local health authority clinics. The local health authority is to be responsible for building, equipment and ancillary staff, but doctors practising from health centres are to be in direct contract with the local executive committee. A new development such as this, if it is to be successful, must not only be the subject of experiment to ascertain the best type of accommodation, but it must also start in proper surroundings.

Improvisation and the adaptation of existing buildings can only in exceptional circumstances provide those additional facilities which a health centre specially constructed for the purpose can make available. Good consulting rooms for doctors and dentists, adequate waiting space for patients, a minor operating theatre or treatment room, proper provision for nurse, almoner, records and clerks (including personal assistants capable of dealing with the doctors' correspondence and typing reports), and adequate arrangements for dealing with telephone messages, can only be provided in new buildings. There is, however, another development which will undoubtedly appeal to the hard-worked general practitioner and which is capable of more general application, and that is the sharing of certain services in common with a group of neighbouring practitioners. The words "group practice" produce in many people's minds the same feeling of uncertainty as the health centre. Group practice is, as American experience shows, capable of the most elaborate organization. In its simplest form it consists of providing a small group of doctors practising in the same area with certain "labour-saving" aids. A central surgery with a clerk-receptionist capable of dealing with records and telephone messages, and nursing assistance for dressings, would be of valuable assistance to many men, particularly those in industrial areas. It should be possible, by agreement with the local executive council, to arrange that a large house (for example, the older type of "the doctor's house on the corner of the street" which proves such a burden to the modern housewife) is acquired and adapted for this purpose. Provided that sufficient consulting rooms are available, independent practice will not be interfered with and such an arrangement would enable an appointments system to work smoothly. If doctors are to play their full part in the new service they must have sufficient leisure to follow up their cases in hospital, advise their lay colleagues on committees, and keep abreast of modern developments in their art. The communal arrangements outlined above would help to provide this freedom. They have the added merit of being immediately practicable if the doctors wish it.

The Minister reaffirmed recently that it is not the Government's intention to introduce a full-time salaried State medical service. Private practice is to continue unrestricted and the acquisition of private nursing homes is not contemplated. Pay-beds in hospitals receive special mention in the Act.

boards, executive councils and local health authorities will be most valuable in ensuring smooth day-to-day working. Finally, there is the voice of public opinion through its mouthpiece, the Press.

The doctor.—It was recognized from the first that the efficiency of the service depended very largely upon the active interest and cooperation of the medical profession, and steps were taken to ensure this when the Act was drafted. In addition to the central advisory committees the Act provides that a proportion of the boards of governors, regional hospital boards and management committees, and executive councils, shall be nominated by medical men. Local medical advisory committees will play an important part in hospital and domiciliary medical services, and local health authorities have power to coopt medical men to the health committee.

It has become almost a cliché to say that the success of the service depends upon the doctors, but it is not enough for the doctors to agree to join the service. If the doctors decide to join, they must enter fully into the organization of the service. Time must be found to take part in all discussions, both central and local. To participate merely as technicians may put back further organized progress in medicine for several generations.

SOME FUNDAMENTAL ISSUES

The organization of *maternity services* has proved to be difficult. Hospital and specialist provision rests, of course, with the regional hospital boards. The provision and supervision of a midwives' service for attending women in their own homes is the responsibility of the local health authority. Any expectant mother wishing to have a private doctor is at liberty to do so provided she is not on his list under the service. But doctors may be needed for domiciliary midwifery either by the midwife requiring aid or at the wish of the expectant mother. Not every doctor wishes to undertake midwifery, nor is every doctor experienced in this work. Maternity work is outside the range of services which the general practitioner is normally required to give under the Act. It is therefore proposed to set up in each executive council area a professional committee known as the "local obstetric committee" to review the obstetric experience of medical practitioners who wish to provide maternity medical services under the Act. This committee will consist of a consultant obstetrician selected by the local medical committee in consultation with the regional hospital board, the medical officer of health to the local health authority, and two general practitioners experienced in obstetrics and nominated by the local medical committee. The extra fees payable for maternity work have now been published.

Health centres have also provoked much discussion. Most doctors in general practice would welcome the relief provided by, for example, a clerk and nurse, but the conception of practice from a common centre is new to English medicine. Dispensary practice dates, of course, from the 18th century, and local authority clinics have been in use for many years, but the

general practitioner has never acquired the North American habit of going to an "office". The section of the Act relating to health centres lays down that they shall provide accommodation for general medical and dental practice in addition to local health authority clinics. The local health authority is to be responsible for building, equipment and ancillary staff, but doctors practising from health centres are to be in direct contract with the local executive committee. A new development such as this, if it is to be successful, must not only be the subject of experiment to ascertain the best type of accommodation, but it must also start in proper surroundings.

Improvisation and the adaptation of existing buildings can only in exceptional circumstances provide those additional facilities which a health centre specially constructed for the purpose can make available. Good consulting rooms for doctors and dentists, adequate waiting space for patients, a minor operating theatre or treatment room, proper provision for nurse, almoner, records and clerks (including personal assistants capable of dealing with the doctors' correspondence and typing reports), and adequate arrangements for dealing with telephone messages, can only be provided in new buildings. There is, however, another development which will undoubtedly appeal to the hard-worked general practitioner and which is capable of more general application, and that is the sharing of certain services in common with a group of neighbouring practitioners. The words "group practice" produce in many people's minds the same feeling of uncertainty as the health centre. Group practice is, as American experience shows, capable of the most elaborate organization. In its simplest form it consists of providing a small group of doctors practising in the same area with certain "labour-saving" aids. A central surgery with a clerk-receptionist capable of dealing with records and telephone messages, and nursing assistance for dressings, would be of valuable assistance to many men, particularly those in industrial areas. It should be possible, by agreement with the local executive council, to arrange that a large house (for example, the older type of "the doctor's house on the corner of the street" which proves such a burden to the modern housewife) is acquired and adapted for this purpose. Provided that sufficient consulting rooms are available, independent practice will not be interfered with and such an arrangement would enable an appointments system to work smoothly. If doctors are to play their full part in the new service they must have sufficient leisure to follow up their cases in hospital, advise their lay colleagues on committees, and keep abreast of modern developments in their art. The communal arrangements outlined above would help to provide this freedom. They have the added merit of being immediately practicable if the doctors wish it.

The Minister reaffirmed recently that it is not the Government's intention to introduce a full-time salaried State medical service. Private practice is to continue unrestricted and the acquisition of private nursing homes is not contemplated. Pay-beds in hospitals receive special mention in the Act.

It is as well to bear in mind that these private beds are of two kinds. There is the so-called "amenity" bed for the patient who desires privacy, and there is the bed for the private patient who elects to obtain the whole of his treatment outside the service. There are two provisos. If a patient needs privacy imperatively on medical grounds he must have it regardless of means. The doctors treating patients in pay-beds must have joined the service.

ANCILLARY SERVICES

It remains to discuss certain ancillary services which, properly organized, will be of inestimable value to the doctor and his patients.

Perhaps most important of all, is the duty laid upon local health authorities to provide an *ambulance service*. It is possible in these days of shortage of men, women and materials to make excuses for many things, but no excuse will avail for the inability to obtain an ambulance in the case of accident or sudden illness. Local health authorities must provide these ambulances, not only for the conveyance of people from their own homes, but also for the hospital service, and they must provide them regardless of boundaries, and free of charge to the patient. The ambulance service includes the provision of cars for sitting cases.

Home nursing.—Section 25 of the Act lays down that it shall be the duty of every local health authority to make provision in their area for securing the attendance of nurses on persons who require nursing in their own homes.

The growth of District Nursing Associations and the great reputation built up within the last sixty or seventy years by the district nurses need no emphasis. On the other hand, it is useless to disguise the fact that the existing district nursing services show great gaps. Highly organized district nursing associations adjoin small and impoverished associations employing only one or two nurses. Again, areas may be entirely uncovered by district nursing associations. Local health authorities must obviously be free to build up the service which they think is best fitted to the needs of their areas. But it is clear that in the great majority of cases they will, at all events at the start, need to make the fullest use of the existing organizations.

On the question of equipment much requires to be done. Some of the district nursing associations have loan cupboards from which the district nurse can take apparatus such as bed-pans, back-rests and bed-cradles to the family requiring them. In the future the demand for this equipment is likely to be much greater and there is little doubt that the local health authorities will need to provide stores of equipment in order that home nursing may be carried out efficiently. Careful thought will also need to be given to the building up of the service to ensure that the doctor can enlist the aid of the district nurse with the minimum of delay. The ideal is for the general practitioner to know the district nurse for his area and call on her direct. This will not always be possible and the superintendent of the home nursing service will have a most responsible part to play in keeping in touch with the general practitioners in the different parts of her area to see that their calls are met immediately.

Section 24 deals with *health visitors* who are to give advice on the care of expectant or nursing mothers, young children, and persons suffering from illness, and also on the measures necessary to prevent the spread of infection.

This definition of the health visitor's duties has given rise to some misunderstanding. In particular, the giving of advice to persons suffering from illness has been interpreted as an infringement of the duty of the family doctor. This is, of course, not the case.

Home helps.—Arrangements are outlined in Section 29 of the Act for the provision of domestic help. The local health authority may make arrangements for providing domestic help for households where such help is required owing to the presence of any person who is ill, lying in, an expectant mother, mentally defective, aged, or a child not over compulsory school age. Here is a much bigger field than appears at first sight. It is fruitless to adopt a short-sighted policy and to say that home helps are not available in sufficient number at the present time to justify setting up this service. The home helps must be made available, and there is undoubtedly a considerable number of middle-aged and elderly women who, if properly instructed, will be only too glad to take on this type of work.

Also linked with these three services is the very important Section 28 dealing with *the prevention of illness and care and after-care in the home*. This is indeed a wide provision and the implications become immediately obvious. No longer should it happen that a patient is discharged from hospital without proper inquiry into the home circumstances. Arrangements will need to be made before discharge from hospital to ensure that the home conditions are suitable to receive the patient, and that the necessary instructions are given for his care and comfort until such time as he is fully recovered.

Dental and ophthalmic services.—Dental care under the service includes emergency treatment as well as conservative dentistry and the provision and repair of dentures. In addition to the free dental service for the general population, priority is to be given to expectant mothers and young children, and the responsibility for arranging this priority service rests upon the local health authorities. Ophthalmic services will include sight testing and the supply and repair of spectacles. It is intended that when the hospital facilities are fully developed, the ophthalmic service will be administered under the supervision of the ophthalmologists as part of the hospital and specialist services. Until that is practicable, arrangements are in hand to provide a supplementary ophthalmic service whereby patients may get their eyes tested, either by medical practitioners with special knowledge and interest in ophthalmology or by the ophthalmic opticians. Dispensing opticians will be responsible for the supply of spectacles. In the supplementary service, glasses will be supplied by the ophthalmic or dispensing opticians.

POSTGRADUATE UNIVERSITY COURSES

It is an essential part of the new service that postgraduate courses should be arranged in conjunction with the parent university. Details of these courses

require to be worked out but it is probable that they will follow four main lines. The short week-end course in a special subject, e.g. obstetrics or pædiatrics, has proved popular in the past with general practitioners. There is also the more extended refresher course lasting for about a fortnight. In addition, there must be provision for the young man wishing to specialize, and also special leave for the consultant wishing to study the methods of his colleagues practising in this country and abroad. Close coordination between the regional hospital boards, the boards of governors of teaching hospitals, and the Universities will be necessary to ensure that these various postgraduate courses are not only interesting but accessible to the busy practitioner.

COST OF THE SERVICE

The cost of the new service with all its requirements in hospital provision, health centres, medical, nursing and ancillary staff will be heavy. It will be met from three sources: first, from State funds, secondly a small proportion of the insurance contributions, and thirdly, in the case of the local health authority services, from the rates as to approximately 50 per cent. of the cost. The individual will therefore pay for the services he receives by direct taxation, through the rates, and by his insurance contributions. A direct charge will, however, be made for privacy in hospital. Local health authorities may make a charge according to the patient's means under the domestic help scheme and also for any arrangements made for the care and after-care of patients in their own home, excluding the tuberculous. For example, a charge may be made for the loan of equipment required for home nursing.

CONCLUSION

In times of stress it is comforting to look back into the past. The 70's of the last century saw the introduction of reforms in public health which were, for that period, as revolutionary as the present social legislation. The effects of the great Public Health Act of 1875 did not become fully apparent until this century, and we cannot attempt to judge the present legislation on the results of the next few years. On Thursday, August 9, 1877, T. Spencer Wells, F.R.C.S., gave an address to the British Medical Association at Manchester. In the course of that address he said: "And what a task lies before the medical statesman! Never in the whole history of our profession have we had so much work to do, such problems to solve, so many human beings dependent for their health on our knowledge and our care". He ended with this quotation: "Look not mournfully into the past. It comes not back again. Wisely improve the present. It is thine. Go forth to meet the shadowy future without fear, and with a manly heart".

SOCIAL MEDICINE IN THE UNITED STATES OF AMERICA

By LOUIS H. BAUER, M.D.

Trustee of the American Medical Association

AND W. W. BAUER, M.D.

Director of the Bureau of Health Education, American Medical Association.

THE term social medicine as employed in this article should not be confused with the vague and misleading term "socialized medicine" which is currently applied in the United States to compulsory governmental health insurance. Social medicine is a broader and more comprehensive term, meaning in essence the relationship of medicine to the social order and the application of medical science to the public welfare.

In presenting the social medicine situation in the United States, an effort will be made to do so factually and without argument. For the British reader, comparison with his own social medicine situation can be made if certain fundamental differences in governmental organization are kept in mind. In the United States there are three levels of government—local, state and national. The constitution limits the national government in its authority within the states. Local government units are created by the state governments and are subject to their control. In Britain, the equivalent of the American state is essentially absent. The United States has no equivalent to the British Ministry of Health, but has instead on the federal level approximately nineteen federal agencies with some relationship to public health; of these the United States Public Health Service comes nearest to being a federal department of health. Yet this important agency has only a status of a subsidiary bureau in a lay-controlled department, the Federal Security Agency. The latter, in turn, lacks cabinet status.

MEDICAL CARE IN THE UNITED STATES

For the purposes of this article the organization of public health and preventive medicine activities will not be considered. Attention will be centred on those phases of social medicine relating to medical care. Only during the past generation has any question arisen about the American system of medical care. That criticism is now levelled at our system is due to the advancement and increased complexity of medical science itself (Bauer, 1947).

The *ten-point programme* of the American Medical Association in the field of social medicine is as follows:—

(1) Minimum standards of nutrition, housing, clothing and recreation are fundamental to good health.

(2) Preventive medical services should be available to all and should be rendered through professionally competent health departments. Medical care to those un-

able to provide for themselves should be administered by local and private agencies with the aid of public funds when needed, preferably by a physician of the patient's choice.

(3) Adequate prenatal and maternity care should be made available to all mothers. Public funds when needed should be administered by local and private agencies.

(4) Every child should have proper attention, including scientific nutrition, immunization and other services included in infant welfare. Such services are best supplied by personal contact between the mother and the individual physician, but may be provided through child health centres administered locally with support by tax funds whenever the need can be shown.

(5) Health and diagnostic centres and hospitals necessary to community needs are preferably supplied by local agencies. When such facilities are unavailable, aid may be provided by federal funds under a plan similar to the provisions of the Hill-Burton Bill.

(6) Voluntary health insurance for hospitalization and medical care is approved, the principles of such insurance plans to be acceptable to the Council on Medical Service and to authoritative bodies of state medical associations.

(7) Medical care, including hospitalization, to all veterans should be provided preferably by a physician of the veteran's choice, with payment through a plan agreed on between the state medical associations and the Veteran's Administration.

(8) Research for the advancement of medical science, including a National Science Foundation, is endorsed.

(9) Services rendered by volunteer philanthropic health agencies should be encouraged.

(10) Widespread education in the field of health, and the widest possible dissemination of information regarding the prevention of disease and its treatment, are necessary functions of all departments of public health, medical associations and school authorities.

PROBLEMS OF MEDICAL SERVICES

Expenditure.—During the last seventy-five years various factors, such as increased medical education, hospitalization, diagnostic procedures, and nursing care, have not only raised medicine from the status of an art to one of both art and science, but have called for increased specialization and further increase in expense. Years of training and experience are necessary to train a competent specialist. Another increase in the cost of medical care is in therapy. Many of the new drugs and biological products are expensive. The time has long passed when the patient can be treated with pills out of the doctor's bag, or by a "shot-gun" prescription filled at the local drug store. These facts are well known to every worker in the medical profession but are not so readily understood by the general public. Individual citizens are likely to see only the increased amounts of their family bills for medical care, and fail to realize that whilst modern diagnostic procedures, hospitalization, nursing care, fees of specialists, and the cost of modern therapy have pyramided the family's *family doctor receives little more to-day than* *ges of* *if the value of the dollar to-day is compare* *receives practically no more.*

In a study of consumer expenditures by the American Medical Association (1946) it was found that the *capita* cost for services of doctors was \$8.15. The

ical S
verag
ita f

dries, glasses and orthopædic appliances was \$8.25. The average *per capita* for other medical expenses was \$6.10, or a yearly total for medical care of \$22.50. These figures were derived from reports in Survey of Current Business (June 1944), a publication of the United States Department of Commerce. The Council also reported that the *per capita* expenditure for recreation was \$34.60; for alcoholic beverages, \$38.70; for tobacco, \$18.00; and for automobiles, \$24.90.

The factors which have been mentioned above as advances in medical progress have also resulted in other unsatisfactory conditions. For example, the necessity for greater diagnostic facilities and hospitals, the greater facilities for postgraduate training, and the greater financial opportunities in cities, have brought about an unequal distribution of physicians.

Distribution of doctors.—There are areas in the country in which there are either no physicians or an inadequate number. There are also areas in which diagnostic facilities and hospital beds are lacking. A young physician starting out is reluctant to go to one of these places. Often they are also lacking in cultural facilities for bringing up his family; the doctor may have difficulty in making a living; and even if these two factors do not operate, lack of proper equipment with which to work makes it impossible for him to practice good medicine. Thus, he either leaves and goes to a more satisfactory locality, or he does what is worse—stays and practices poor medicine.

In combination then, we have a problem which did not exist seventy-five or even thirty-five years ago. Namely, *how are we to make a better distribution of medical care at reasonable cost?* Various solutions have been suggested, but all of them must be evaluated practically in terms of conditions as they exist, and in the light of the realization that *quantity* of medical care, unless it is also of high *quality*, cannot solve the problem.

Rural areas.—It is true that the trend of physicians toward cities has depleted the supply of doctors in rural areas. But rural medical care is one of our greatest problems for other reasons as well. The higher mortality and case rates for infectious and preventable diseases in rural areas are directly related to other deficiencies as well as to the lack of physicians. For example, rural areas are notably lacking in sanitation, improved water supplies, the diagnostic and hospital facilities which have already been mentioned, and in public health facilities. Nearly half the counties of this country do not have full-time public health departments. The problem of rural medical service is economic and social as well as professional. Much the same statement could be made concerning the problem of medical care in under-privileged, non-rural areas. A marked economic factor plays a large part in the production of the need for medical care. With inadequate housing, clothing and nutrition, much medical care is required which would not be needed if these other factors did not pertain.

A deficiency also exists in *public education* about health facilities which are now available, with the result that many facilities are not used to their utmost.

In consideration of any programme of medical care, the indigent present

a problem. Until recently, this group has been almost entirely dependent upon private philanthropy and the charity of the physician. During the depression this became too great a load and it has been necessary for the government to appropriate funds to help take care of these patients.

The *availability of hospital beds* must be considered—not only for general use, but for the care of tuberculous and mental patients. At the present time, the total number of hospital beds in the country is above the minimum needed to care for our people. However, government hospitals have 78 per cent. of the total bed capacity, but account for only 39 per cent. of the admissions. In mental institutions 97 per cent. of the beds are government controlled, but these account for only 1.5 per cent. of the admissions for 1945. There are approximately 80,000 tuberculosis beds, most of which are in government controlled hospitals. We have 3.5 beds per 1000 in general hospitals. The ideal number is figured as 4.5 beds per 1000 and the minimum safe number is 2.5 per 1000.

There is no denying, however, that there is a shortage of hospital beds in certain areas of the United States, and that this shortage seriously affects the medical care situation in those areas. About 40 per cent. of the counties in the United States have no general hospitals. All but thirteen of these counties, however, are no more than thirty miles from a general hospital and, in these days of good roads, that is not far. Of these thirteen counties, only five have a population of more than five persons per square mile; which leads us to the conclusion that in selecting places to construct hospitals, attention should be paid to the needs of the individual community. Full use of existing facilities should be made first; extension of existing facilities where needed, and construction of new hospitals where none exist and the need for them is apparent must next be considered.

MORBIDITY AND MORTALITY RATES

At the present time, in spite of the problems which we have to face, the United States has the best health record of any nation in the world. Our general mortality rate is lower than that of any other large country; our morbidity rate and our maternal and infant mortality rates compare favourably with every other country. These rates are constantly going down, and even during the recent war, when there was a shortage of physicians for the civilian population, the health of the country continued to improve. Since the war, our ratio of physicians to the population as a whole is 1 to 750. This ratio varies, of course: in rural districts it is about 1 to 1,600; in large cities, 1 to 500.

Selective Service statistics have often been used to deny the good health of this nation, and to blame the lack of medical care.

The actual facts are that of the 4,217,000 rejected, some 443,800 were rejected for manifestly disqualifying defects, such as total blindness, total deafness, deformity, loss of arms or legs, and so forth. It is evident that all the medical care in the world could not have rendered these individuals available for military service.

Another 701,700 were rejected for mental disease. In this connexion it might be noted that 90 per cent. of all mental institutions are under government control. Another 582,100 were rejected for mental deficiencies. This includes the idiots, imbeciles and morons, and about 250,000 who were illiterate. Here again medical care seems scarcely responsible, and it should be remembered that we have had compulsory education for many years.

Some 283,000 were rejected for syphilis. There is probably no disease for which there has been more education of the public, more money spent, and more free clinics established. All this number could have been treated adequately had they so desired, and certainly the lack of availability of medical care cannot be blamed for their being unavailable for military service.

About 212,700 were rejected on account of their eyes. These doubtless, to the greater extent, consisted of those with defective vision. It is doubtful whether medical care could have made many of these men available for military service.

Another 113,200 were rejected for tuberculosis. Again, institutional treatment for tuberculosis is largely under government control, and is available without cost to anyone who desires it.

If we accept all the rest of those rejected, we have only about 1,500,000 instead of over 4,000,000 rejected for physical reasons who might have been salvaged. And even of these, we find that over 273,000 were rejected for cardiovascular disease, which we do not yet know how to prevent; and 238,400 were rejected for hernia. Incidentally, many of these hernia cases were offered the opportunity to have their hernias corrected, and they refused.

In light of analysis, the Selective Service figures are not valid proof that the health of this country is in a bad way. However, they have been used in such an attempt, as the question of medical care which should be confined to the field of medical economics has become a political football.

For more than twenty-five years the government has made gradual inroads into the private practice of medicine. Where these inroads pertain to public health measures they are satisfactory, so long as politics is not a factor. Most public health measures could not be carried on by the private practitioner, as they involve sanitary engineering, group protection and the police power. Many diseases are prevented by public health measures which must be on a community, and not on an individual, basis. Certain diseases, such as tuberculosis and mental disease, can be treated more or less on a group basis. Even here, however, government hospitals for the care of these individuals are not up to the standard of our best private hospitals.

THE AMERICAN MEDICAL ASSOCIATION HEALTH PROGRAMME

Most other countries have *compulsory sickness insurance* as a governmental measure. Bills presented for enactment in this country have been based upon these European systems, which Americans do not consider satisfactory. They have failed to recognize the fundamentals of a satisfactory system for delivery of good medical care. An over-all solution without regard to primary needs has been offered. Instead of giving attention to those factors which are not identical in different areas of the country, they have suggested treatment of every section of the country alike, regardless of need. Basic deficiencies are not attacked, nor is specific treatment offered for specific ills. Dependency, red tape, inefficiency and regimentation are encouraged.

a problem. Until recently, this group has been almost entirely dependent upon private philanthropy and the charity of the physician. During the depression this became too great a load and it has been necessary for the government to appropriate funds to help take care of these patients.

The *availability of hospital beds* must be considered—not only for general use, but for the care of tuberculous and mental patients. At the present time, the total number of hospital beds in the country is above the minimum needed to care for our people. However, government hospitals have 78 per cent. of the total bed capacity, but account for only 39 per cent. of the admissions. In mental institutions 97 per cent. of the beds are government controlled, but these account for only 1.5 per cent. of the admissions for 1945. There are approximately 80,000 tuberculosis beds, most of which are in government controlled hospitals. We have 3.5 beds per 1000 in general hospitals. The ideal number is figured as 4.5 beds per 1000 and the minimum safe number is 2.5 per 1000.

There is no denying, however, that there is a shortage of hospital beds in certain areas of the United States, and that this shortage seriously affects the medical care situation in those areas. About 40 per cent. of the counties in the United States have no general hospitals. All but thirteen of these counties, however, are no more than thirty miles from a general hospital and, in these days of good roads, that is not far. Of these thirteen counties, only five have a population of more than five persons per square mile; which leads us to the conclusion that in selecting places to construct hospitals, attention should be paid to the needs of the individual community. Full use of existing facilities should be made first; extension of existing facilities where needed, and construction of new hospitals where none exist and the need for them is apparent must next be considered.

MORBIDITY AND MORTALITY RATES

At the present time, in spite of the problems which we have to face, the United States has the best health record of any nation in the world. Our general mortality rate is lower than that of any other large country; our morbidity rate and our maternal and infant mortality rates compare favourably with every other country. These rates are constantly going down, and even during the recent war, when there was a shortage of physicians for the civilian population, the health of the country continued to improve. Since the war, our ratio of physicians to the population as a whole is 1 to 750. This ratio varies, of course: in rural districts it is about 1 to 1,600; in large cities, 1 to 500.

Selective Service statistics have often been used to deny the good health of this nation, and to blame the lack of medical care.

The actual facts are that of the 4,217,000 rejected, some 443,800 were rejected for manifestly disqualifying defects, such as total blindness, total deafness, deformity, loss of arms or legs, and so forth. It is evident that all the medical care in the world could not have rendered these individuals available for military service.

of nutrition, housing, clothing and recreation are recognized as fundamental to good health, there will always be an increased necessity for medical care among certain groups of people, which would be entirely unnecessary if these minimum standards were maintained. This is not a medical problem, but an economic one of the community. The responsibility is primarily on the individual, but community effort compatible with the maintenance of free enterprise should be encouraged with governmental aid where necessary. Furthermore, much disease can be prevented if we have preventive medicine available to all persons; such services being rendered by professionally competent health departments, previously discussed.

In the case of the indigent, medical care for those unable to provide for themselves should be administered by local and private agencies, preferably by a physician of the patient's choice. Here again, those communities which are unable to finance the project should be helped from the outside. This particular factor, in the case of states, is met by the so-called Taft-Smith-Ball-Donnell Bill, which provides for increased grants-in-aid for the medical and hospital care of the indigent.

This bill also provides for subsidies to physicians practicing in areas which, without such payments, would be unable to provide sufficient income to attract them. It also provides for the payment in whole, or in part, of the premium to any voluntary health, medical and hospital insurance or insurance funds not operated for profit. This would result in the indigent and those of low income being able to obtain adequate medical care without thought of the cost. Whilst the original Taft Bill was not intended as a final solution to the problem, but was introduced primarily as a counter-measure to the Wagner-Murray-Dingell Bill, nevertheless, the 1947 version has the makings of a satisfactory solution of the problem of the indigent and the medically indigent.

As to the *prenatal and maternity care* necessary, this should also be administered through the physician of the patient's choice, and proper facilities should be available to all mothers. Again, appropriations can be made by the Federal government to meet the shortages of local communities. Child welfare, including nutrition, immunization and other services, is best supplied by the individual's physician, but in the case of the indigent, there is no objection to this being provided by child health centres which are administered locally, with the support of tax funds. Where the need is shown, these funds will have to come from the Federal government. The Hill-Burton Act, it is hoped, will do much to provide the necessary health and diagnostic centres for those communities now lacking them. These funds will be available for the next five years, and it may be necessary to make them available for a still longer period and possibly to increase the extension of the Federal government's contribution. Not only will this make the necessary facilities available, but it will help towards a better distribution of physicians by giving them the facilities for practicing good medicine.

Compulsory sickness insurance is undeniably a step towards national socialism.

The American Medical Association realizes the need for improved medical care and is active in support of measures which can attain it without lowering the quality of care which our people now enjoy. The Association is a democratic body which is concerned with the advancement of scientific research. It has done more to improve the standards of medical care both within and without the hospital, to improve medical education, and to protect the public against nostrums and quackery than all other organizations combined. The opposition of the American Medical Association to the bills proposed has not been due to lack of progressiveness, but to the contrary.

The Association has backed the gradual evolution of the *voluntary insurance system* in the United States. This system, which first started with *group hospitalization insurance*, had a slow growth at the beginning, but is now progressing rapidly. To-day there are over thirty million persons covered by Blue Cross Hospitalization insurance, and several million more protected against hospitalization through industrial or under private commercial insurance.

Medical care insurance was started later. Progress was slow because of lack of actuarial background. After much experimentation, some of which was undertaken by local and state medical societies, two general types of plans have emerged: one involving cash indemnity and the other medical service. Approximately nine million persons are now protected by prepaid medical care plans. The original ideal of complete medical coverage has not been successful to date. First, because of its unpredictable costs, and secondly, because the public has shown no great interest in purchasing it. However, such plans are growing and to some extent are even reaching into rural areas, through the cooperation of farm organizations, such as the National Grange.

Contracts permitting the establishment of health and welfare funds in the mining industry have recently been enacted. Conferences have been held by the medical profession with representatives of the mining industry, and an association of mining physicians has been organized and emphasis placed on the development of high standards of medical care, for which the physician should receive adequate remuneration. It seems quite possible that health and welfare will be important factors in all future collective bargaining.

The Association has approved the principle of participation in, and support of, all industrial health activities jointly by management and labour; and that the scope, technique and character of support of medical and health services for workers should be developed and approved as a composite plan based on collaboration between management, labour and medicine.

Economic factors.—The Association insists that unless minimum standards

NEW ZEALAND STATE MEDICAL SERVICE

By A. E. PORRITT, C.B.E., M.Ch., F.R.C.S.

Surgeon to H.M. the King; Surgeon, St. Mary's Hospital.

Experientia docet! Over twelve years ago, in December 1935, a socialist government came into power in New Zealand, with the expressed policy of "state control of the means of production, distribution, and exchange". One of the springiest planks in its platform and one of its more ideological concepts was the nationalization of medical services. The subsequent experiment—essentially a social one carried out on the public of the Dominion—has gone on for the past few years, and in view of contemporary happenings in this country to-day it would seem of more than passing interest to study the results. To obtain a reasonable perspective, the background and environment of the experiment must be briefly considered.

New Zealand, a young Dominion, has always, at any rate since the birth of this century, been health conscious. It is worthy of note that a Ministry of Health has existed there since 1900, whereas in this country the first Minister of Health was not appointed until 1919. The country itself, with a population now of barely $1\frac{3}{4}$ millions, possesses many attributes which should ensure a high standard of health. The climate is temperate, with ample sunshine; there is no overcrowding and virtually no slums; the majority of the people live an outdoor life with plenty of fresh air, and they come from a virile stock; the food is ample and good, and facilities for recreation, both mental and physical are readily available. Hence it is all the more surprising to find that the New Zealand birth rate is only a little higher than in other parts of the Empire; that its sterility and abortion rates are high; that dental caries is rife; that the suicide rate is high; and that it possesses an unenviable number of large mental institutions.

That a very definite health problem existed therefore before 1936 cannot be denied, but it would seem to have been centred rather in preventive medicine than in clinical practice. At this door of preventive medicine most of the faults could be laid, although inside the medical house could be found various organizational defects (in the hospitals; between Public Health Departments and doctors; perhaps between doctor and hospital), and there is no doubt that for a proportion of the community—a small one—full medical facilities were hard to come by. Any official backing for research was conspicuous by its absence, and to all intents and purposes, still is.

The profession was at this time, however, a happy and an efficient one, and the standard of medical education high—facts vouched for and appreciated by this country. In some fields, e.g. child welfare, New Zealand was an acknowledged leader in world medicine. The hospitals then were approximately half state-subsidized and half supported by local authorities. They provided in 1936, 8.4 beds per 1000 of population—a rate equalled only by Australia and Norway. Since then a world's record has been

The Veterans' Administration is now placing contracts for the care of veterans with Service disabilities, with medical societies and medical care plans so that the veteran may be taken care of by his own physician in his own community, both at home and in the hospital. This is a great step forward, and will result in a much better type of medical care being afforded the veteran than has heretofore been the case. The only difficulty in the programme at present is that there is a shortage of civilian hospital beds, which it is hoped will soon be taken care of through the carrying out of the Hill-Burton Act.

Another item in the programme of the American Medical Association pertains to *medical research*. Various bills were introduced into Congress for the establishment of a National Science Foundation. Coordination of medical research will be excellent, but it is essential that it be headed by a scientific board, and not by a politically appointed director. Recently, it has been suggested that there should be a group of fifty scientists who would select their Director. Such an arrangement would keep politics out of science and research.

Voluntary societies.—We have numerous volunteer philanthropic agencies, foundations and funds which are related to the practice and science of medicine. The Association feels that the work of these organizations should be tied in with that of organized medicine so that there will be no duplication of effort. Suggestions have been made to amalgamate these organizations, but their independence should be maintained. Possibly some of their fund drives could be united, and the funds allocated according to their immediate needs.

The final point of the American Medical Association ten-point programme pertains to public education in the field of health. Departments of public health, medical societies, and school authorities should give the highest possible dissemination of information regarding the prevention and treatment of disease, so that the public will be fully aware of what can be done and what facilities are available to do it.

Enactment of the Taft-Smith-Ball-Donnell Bill, with certain revisions, will materially assist in the carrying out of the American Medical Association ten-point programme. A properly controlled science and research bill is the only other legislation which is at all essential at the present time.

When all these conditions are met, the fulfilment of such a programme will meet the needs of the country for a better distribution of medical care, and will make entirely unnecessary the enactment of any paternalistic legislation with its second-rate care, red tape, inefficiency and political interference as is involved in the Wagner-Murray-Dingell Bill or any other form of compulsory sickness insurance.

Reference

Bauer, L. H. (1947): "Private Enterprise or Government in Medicine," Springfield, Illinois.

possessing man and woman in New Zealand receives a degree of health service at the price of 1s. in the pound. It may fairly be said at this stage that the very nature of the scheme, its piecemeal character, has made it difficult to work, and this, combined with an unfortunate absence of appreciation of the value of consulting the profession itself on matters regarding it, of which even the most astute and ideological politician is woefully lacking in knowledge, have undoubtedly to some extent accounted both for its somewhat chequered career and equivocal results.

After seven years of trial it would seem that some assessment of such an important national experiment should be possible, but unfortunately the facts available serve only to illustrate a part of the picture. Financial figures and hospital statistics are definite enough, but the reactions of the profession and the public are much more difficult to evaluate, whilst the effect on the efficiency of medical service, on ethical standards, and on the national future of its doctors and its people can, at any rate for many years yet, be only guess work.

THE FINANCIAL ASPECT

The hard facts of finance can be clearly faced. The word "free" is most certainly a misnomer of the most eulogistic kind. The medical part alone of the social security benefits cost the country $5\frac{1}{2}$ million pounds in 1945/46. In the following year this had risen to £3 12s. 6d. per head (as against a previous highest of £3 5s. 5d.), and the figure is still rising. Of this sum approximately 25 per cent. is expended on drugs—a figure of about $1\frac{1}{2}$ million pounds annually. In 1943, $3\frac{1}{2}$ million prescriptions were dispensed at government expense; in 1945 almost 5 million, and in 1946 practically 6 million (or an average of 4 prescriptions per head of population per year). There is little doubt that, apart from the greatly increased cost of drugs to-day, these figures show an unnecessary enjoyment of poor health on the part of the New Zealand public. It is selective enjoyment, however, as in 1946, 1 per cent. of all prescriptions were valued at over £1! That these outgoings are considerably in excess of government estimates is proved by the fact that in 1945-6 the social security tax required an addition of £7 millions from consolidated revenue to meet expenditure and in 1946-7 this extra assistance involved a subsidy of £18 millions! These are figures which in a small country like New Zealand must give the powers that be most seriously to think. New Zealand certainly pays dearly for its health services.

WHAT ARE THE RESULTS?

What advantages accrue to the various sections of the community?

The public has had access to the profession unrestricted by financial considerations. For a small minority this has undoubtedly been a great boon; for the majority it has meant rather more cursory attention than heretofore, and undeniably longer delay in obtaining hospital facilities. That drugs have been freely available would seem to pander chiefly to the professional chronic—those who make a visit to the doctor one of their chief interests in

achieved: in 1944, 10.2 beds per 1000 were available and still there are complaints of crowded hospitals and shortage of staff, whilst big building projects are being mooted. This may be a reflection on the national health or on the national health service—or both.

GROWTH OF THE HEALTH SERVICE

Reverting to historical facts: the Government in 1938 began to introduce its Social Security Legislation. This not unnaturally was political in conception but, as it automatically brought into contact those immiscibles, medicine and politics, it was unfortunate that the advice of the profession should have been ignored. The various measures which have built up the existing system in New Zealand were, however, introduced piecemeal, chronologically as follows:—

April 1939: Free mental hospital treatment was instituted.

July 1939: Free hospital treatment as a whole came into force, and with it the passing of the honorary medical staffs. Since then all hospital staffs have been at least partly state-paid. Figures prove very conclusively that the demand for hospital treatment has steadily risen since this date, the reasons for which will be discussed later. But the fact remains, and in the absence of any payment by patients the drain on the state purse becomes heavier each year.

November 1939: Free maternity service was introduced, after an initial abortive attempt in May, which was strongly resisted by the profession.

December 1940: A contract capitation scheme for general practitioner service became available. This allowed the patient to sign a contract with the doctor of his choice, by which the patient received general medical benefits and the doctor 15s. per head (plus certain mileage costs) from the Social Security Fund. This scheme, although still extant, proves equally unpopular with doctor and patient alike.

March 1941: Free out-patient treatment at hospital was instituted. As will be gathered from remarks on hospital services above, this provided such an influx of patients that facilities were entirely inadequate and methods of restricting attendances had to be introduced locally.

May 1941: Pharmaceutical benefit was authorized, and a "New Zealand Formulary" introduced. The repercussions of this scheme will be considered later, but it can fairly be said that the temptation to secure something (and that, material) for nothing has not been neglected. There is no reason to suspect that human nature is different in New Zealand from anywhere else in the world!

July 1941: A free X-ray service was initiated.

November 1941: General medical services (i.e., of general practitioner, not consultants if seen outside a "free" hospital) were made available. These were on a "fee-for-service" basis, this fee at first being 5s., raised very soon afterwards in response to the demands of the profession to 7s. 6d.

To date, no further additions have been made, although the introduction of free laboratory and physiotherapy services seems imminent, and the institution of a "consultant service" is being widely discussed on both sides. It will thus be seen that the New Zealand service provides from state funds (not "free", as so many of the laity in New Zealand as well as in this country appear to imagine):—

(a) A general practitioner service.

(b) Maternity service (not only medical fees, but even part payment of private nursing home fees are met).

(c) Pharmaceutical benefit (except for certain specified drugs, such as the more expensive hormones and vitamins).

(d) Hospitalization (either general or mental, in-patient or out-patient, with radiological facilities when required).

It is worthy of note that at the moment such vitally important problems as medical education, research facilities, hospital planning, nursing, and group practice have received no consideration.

Such, then, is the system by which every wage-earning or income-

signs the doctor's claim form for 7s. 6d. per act (consultation, visit, certificate), these claims being forwarded *en bloc* monthly to the Ministry. This is obviously the most pernicious system, as it allows the doctor to deal with anything up to 80 patients a day, of whom any that are difficult or time-consuming are hospitalized, and is an open invitation to over-visiting and over-treatment. It is estimated that 40 per cent. of the profession use this method, and it is amongst this group that there lies the danger of lower professional standards, both ethical and professional. One firmly believes that those who "flog the 7s. 6d. consultation fee to death" are in fact very few in number, but the fact that the scheme offers the possibility of such abuse is very much in its disfavour.

(3) The Refund Scheme by which the practitioner charges the patient his usual fee (e.g. 10s. 6d.), and provides him with a certificate by which he can reclaim from the government. More than 40 per cent. of the profession adopt this method which is undoubtedly the fairest and least open to abuse.

(4) The "Token System"—a mixture of the two previous methods, by which the patient both signs a certificate allowing the doctor to reclaim his 7s. 6d. and pays himself the balance of the fee. This would seem to have all the disadvantages and none of the advantages of methods 2 and 3.

(5) Whole-time salaried service. This is offered chiefly in outlying and sparsely populated districts, especially those with a high proportion of poor patients. It accounts for little more than 1 per cent. of all practitioners.

These various methods of remuneration express as well as any number of words the present alignment of the New Zealand general practitioner service, and it would seem reasonable after several years of trial that the best of these various methods should now be universally adopted. Only so can the Minister of Health be saved from again having to make such a significant admission as "it cannot be gainsaid that conditions prevailing during recent years have in some cases brought about a serious lowering of the quality of medical services".

Of the hospitals, facts and figures already quoted will show that as a secondary effect of the rest of the scheme they are grossly overcrowded, overworked and understaffed—a position of affairs which in no way reflects either on the efficiency of their organization or on the national health.

CONCLUSION

Looked at in perspective the New Zealand scheme seems so far to have suffered from a too hasty conception and a somewhat haphazard institution. Its very incompleteness seems to indicate a lack of long-term planning. It would appear to have done a little good to a minority of patients, a little harm to a minority of doctors, and to be a most costly national experiment. One can hardly expect governments to be good judges of human nature—it is not really their business. But if, for probably very worthy even if political reasons, they must indulge in such pursuits as the nationalization of such an essentially personal relationship as that of doctor and patient, it is hard to imagine why they try, and continue to try, to effect their ends without the fullest consultation with, and cooperation of, those principally concerned.

The New Zealand experiment properly handled might still bear good fruit—it should most certainly provide a crop of valuable data, if studied in detail, for those in the process of launching a similar system. Again—*experientia docet?*

life. Superficially, and in view of the expense involved, the patient would not seem to be getting adequate return for his money. In all fairness he would not, however, seem to be suffering much detriment, except in so far as the national character is being affected. To be on the other side of a "rush bargain-counter for bottles" or the recipient of "slot-machine medicine" cannot really be conducive to the right development of national character, from either the physical, mental or moral aspect. To suggest, however, that the scheme is unpopular with the public would probably be quite untrue. As in industry, any arrangement by which the employee can indulge in unchecked waste and the employer in selfish profiteering is bound to find many adherents. Surely though, it is a right royal and rapid road to bankruptcy—bankruptcy not only of national finance but of national values.

Of the New Zealand doctor it is both easier and more difficult to write. Most of them belong either in fact or in principle to what the present government has dubbed that "hopelessly conservative trades union"—the B.M.A. Most of them continue to practice under a regime which age-old tradition makes them feel is an unnecessary interference with their professional duties, in exactly the same way and with exactly the same ethical code as before the days of a State Health Service. Most of them are relatively prosperous; many have more leisure than heretofore. But this is a generation of doctors with a tradition behind them—not only a New Zealand tradition but a tradition of all the famous medical schools of this country. The deleterious effect will come insidiously as the years pass and generations of doctors take up practice who know only service by set hours, by multiple certification, by standardized hospitalization. At the moment New Zealand is said to be teaching almost twice as many medical students as she requires. The result—already evident to some degree—will be loss of incentive, the levelling to mediocrity of individual personality, the absence of men who have taken higher degrees and who can be leaders of their profession. Practice in New Zealand has recently been called by a New Zealand doctor "humiliating" in that it is founded rather on the number than the quality of acts done. It is undoubtedly a fact that the more certificates a doctor produces, the bigger his practice and the greater his income. Only an inherently high moral standard can counteract such a set of circumstances. At the moment 25 per cent. of doctors receive more than £3000 per annum from government refunds (one or two over £10,000).

THE DOCTOR'S REMUNERATION

A doctor in New Zealand to-day may receive remuneration in one of the following ways:—

(1) He may have a panel and a contractual agreement with his patients for whom he receives 15s. per head per year (December, 1940 scheme). It is estimated that only about 2 per cent. of doctors avail themselves of this method, which is open to all the well-known abuses (e.g. touting by trade union secretaries for individual doctors; no correction of lists of patients who have died, left the country or been confined to mental institutions; hospitalization of chronics).

(2) Direct claim, by which the patient (without any direct financial responsibility)

Other periodicals had long been dead: the *Medical Times* seventeen years, the *London Medical and Physiological Journal* thirty-five years, and the *Medico-Chirurgical Review* some sixty years. At a considerably later period the partition of medicine into "more and more plots of intensive cultivation" (N. G. Horner: *Brit. med. J.*, 1932, ii, 374) led to the founding, one after another, of specialist journals.

The original publishers of *The Practitioner* were Macmillan and Co., and the joint editors were Francis Edmund Anstie, M.D., F.R.C.P., senior assistant physician at the Westminster Hospital, and Henry Lawson, M.D., F.R.C.P., assistant physician at St. Mary's. The latter retired from the editorship after a year, and Anstie remained sole editor until his death in 1874 at the early age of forty-one.

THE MEDICAL BACKGROUND

The following extracts from the Preface to the first volume (July-December, 1868) may here be quoted, as they give a vivid and authoritative picture of the medical background of this period, described by Garrison as the age of therapeutic nihilism:—

"It is admitted on all hands that the present state of Medical Science is in one respect most unsatisfactory. While our knowledge of the facts of disease, as well as of the facts of healthy physiological life, has made great progress of late years, Therapeutics, or the science of healing, has remained very nearly where it was when Rousseau exclaimed, 'Laissez-moi mourir, mais ne me tuez pas'. It is true that in the way of mere destruction of old delusions as to the infallibility of certain methods of treatment, much has been done; and it is also true that by purely empirical inquiry we have got possession of a few remedies—such as cod-liver oil, chloroform, iodide of potassium—which are of the greatest value; but it is none the less certain that an *exact* knowledge of the mode of handling remedies does not exist. Upon this point we shall not be accused of exaggeration, since we can produce the highest authority for our statement. Sir Thomas Watson made the following remarks in opening the First Session of the Clinical Society: 'Certainly the greatest gap in the science of Medicine is to be found in its final supreme stage, the stage of Therapeutics . . . We know tolerably well *what* it is we have to deal with, but we do not know so well, nor anything like so well, *how* to deal with it. . . . We want to know distinctly what is the action of drugs, and of other outward influences, upon the bodily organs and functions; for every one now-a-days, I suppose, acknowledges that it is only by controlling or directing the natural forces of the body that we can reasonably hope to govern or guide its diseased actions. To me it has been a life-long wonder how vaguely, how ignorantly, and how rashly drugs are often prescribed'.

"It is difficult to exaggerate the weight and significance of these words, or the urgency of the need to which they point. There can be no doubt that they have aroused a lively interest in an unjustly neglected but all-important branch of Medical Science; and that henceforth medical men will feel compelled to take into serious consideration the principles on which they proceed in the administration of medicines. . . . *The Practitioner* will appear monthly, and will thus supply the most recent information obtainable on all subjects connected with the application of remedies for disease; and as its bulk of matter will not be great, it is hoped that busy men will be able to master its contents without difficulty. It is proposed that each number shall contain a series of short original articles upon special subjects in Therapeutics; a brief *resumé* of the more interesting items of treatment recorded in the foreign journals; short reviews of important works bearing on treatment; a brief

THE PRACTICE OF MEDICINE EIGHTY YEARS AGO

A REVIEW OF THE FIRST VOLUME OF *THE PRACTITIONER*

By W. R. BETT, M.R.C.S., L.R.C.P., F.R.S.L., F.S.A. Scot.

The Practitioner was born in a memorable year. In 1868 Charles Darwin published "The Variation in Animals and Plants under Domestication"; Eduard Pflüger founded his *Archiv für die gesamte Physiologie*, quickly to become the most popular journal on that subject in Germany; Hans Wilhelm Meyer of Copenhagen gave the first clinical description of adenoid vegetations; Karl Kahlbaum suggested catatonia as a separate disease process; Hering and Breuer defined the rôle of the vagus in self-regulation of respiration; James Lenox founded the Presbyterian Hospital in New York.



Colophon on cover of *The Practitioner* 1868.

It was also the year of the English Pharmacy Act against the unlicensed sale of poisons. When the first number of *The Practitioner* made its appearance in July 1868, it had as its subtitle "A Monthly Journal of Therapeutics". With volume 12 this was changed to "A Journal of Therapeutics and Public Health", and with volume 54 to "A Journal of Practical Medicine". The *Lancet* was then in its forty-fifth year, and the *Glasgow Medical Journal* in its fortieth year. The *Edinburgh Medical Journal* had been started thirteen years previously, and the *British Medical Journal* on January 3,

1857, as the continuation of the *Association Medical Journal* (1853).

The following advertisement for the *British Medical Journal* appeared in the first volume of *The Practitioner*.

"The *British Medical Journal* (Journal of the British Medical Association). Edited by Ernest Hart, Esq., Ophthalmic Surgeon and Lecturer at St. Mary's Hospital, London. Published Weekly: 37, Great Queen Street, Lincoln's Inn Fields. Price to Members, Free by Post, One Guinea Annually. This Journal, published by the *British Medical Association* (numbering now four thousand of the élite of the profession), is admitted to be in all respects equal to journals seeking commercial profit, and having a much higher annual subscription".

The *Medical Press and Circular*, born in 1839, had appeared under its new title in Dublin two years previously, and moved to London in the year of *The Practitioner's* birth. The *Dublin Journal of Medical and Chemical Science*, born in 1832, in 1846 changed its name to the *Dublin Quarterly Journal of Medical Science*, and in 1872 to the *Dublin Journal of Medical Science*. Since 1922 it has been known as the *Irish Journal of Medical Science*.

prejudice, and gave alcohol a cautious but a fair trial in acute inflammations, especially pneumonia, and reported very favourably of the results of his experiments. M. Gingeot, the author of the volume before us, is one of the most distinguished of M. Béhier's pupils . . . He comes to the conclusion that alcohol may be used in a large number of acute diseases, and even during the pyrexial stage, with benefit; and he is also of the opinion that the treatment answers as well in the case of children as in that of adults". There is also a review of G. Pécholier's book "*Sur l'Emploi de l'Alcool dans le Traitement de la Pneumonie*", 1867.

In the August number an annotation on "Intestinal Obstructions treated by Electricity", taken from the *Bulletins de la Société Médicale d'Emulation* (this journal, we must confess, is new to us) makes astonishing reading. M. Krishaber is reported to have urged on practitioners the advisability of having recourse to electricity in such cases: "The intestine, from having made several ineffective efforts to expel the obstruction, becomes as it were exhausted and ceases entirely to contract. Then the continuous passage downwards of the contents of the intestine above the obstruction, renders this latter greater than before. Hence . . . there is all the more probability of electricity being attended . . . with most beneficial results".

The opening sentences in Alfred Meadows's article "On the Therapeutical Uses of the Ergot of Rye", contributed to the September issue, are of some interest and bear repetition: "It is not a little remarkable, and certainly does not say much for our knowledge of Therapeutics, that we should be in comparative ignorance of the *modus operandi* of some, and in complete ignorance of that of many, of our most valuable medicines. Indeed it may safely be said that, excepting those drugs which act chemically, there are very few whose physiological or therapeutical action is clearly understood". It may here be recalled that although ergot in the induction of labour was first used in America by John Stearns in 1808, the scientific history of the drug only dates from 1920 when Arthur Stoll extracted ergotamine from ergot.

In the October number attention is arrested by the title of a paper by Thomas Buzzard "On the Interception of the Epileptic Aura by Blistering". Four cases are reported, "one on account of the happy result of the treatment applied, and the other three because of the very curious influence which was apparently exerted by the blisters upon the site of the epileptic aura".

"On Blood-Letting as a Point of Scientific Practice" is the title of a presidential address delivered by the great Benjamin W. Richardson, M.D., F.R.S., before the Medical Society of London, and published in the November number: "I cannot open this address more plainly than by expressing the conviction that blood-letting, when the time and case for resorting to it are understood, is one of the most truly scientific remedies we have at our command; that it produces effects as patent to the eye, as convincing to the reason, as any known remedial measure. I believe that

sketch of Practical Medicine for the month, as observed in the London and provincial hospitals; a department for Notes and Queries, in which correspondents may ask, and obtain replies to, questions in reference to problems on which they desire to have the opinions of other medical men; and finally, a bibliographical list for the month".

THERAPEUTICS IN 1868

A rapid glance at the Original Communications included in the July number is both instructive and stimulating. Dr. Maisonneuve, Surgeon to the Hôtel Dieu, Paris, writes on "The Treatment of Wounds by Pneumatic Aspiration"; J. Russell Reynolds, M.D., F.R.C.P., "On the Therapeutic Uses of Bromide of Potassium", which "became a 'fashionable' medicine a few years ago; and, like some of its predecessors in the circle of fashion, was soon overrated, and misapplied; it failed to do in all cases what it had been said to do in some; occasionally it appeared to be mischievous, and often it seemed inert; and so, within the last few months, there have arisen those who entertain doubts as to its possessing real value in the treatment of disease". The third article "Faradisation in the Treatment of Paralysis" comes from the pen of J. Netten Radcliffe, M.R.C.S., Medical Superintendent of the National Hospital for the Paralysed and Epileptic, who complains that "the use of electricity as a therapeutic agent, and in pathological investigations by English medical practitioners, lags much behind the knowledge acquired of its diagnostic and remedial value. This arises less perhaps from any disposition to underrate the worth of the agent in medicine than from certain errors of manipulation in its application to the diagnosis and treatment of disease". An interesting paper follows by Sidney Ringer, M.D., Professor of Therapeutics in University College, entitled "On the Employment of Glycerine of Tannin". The writer "is induced to make a few remarks on the employment of this preparation of tannin, as it appears to be but little known, and of course but little used, while, in his opinion, it proves of great service in many diseases". Dr Anstie contributes an article on "The Hypodermic Injection of Remedies", based on ten years' experience. At that time this method of giving drugs was apparently not yet very popular, and it is interesting to find the Editor confessing "I not infrequently meet practitioners who will not admit that there can be any particular advantage in it which the old way of giving medicines does not offer, and who are, moreover, possessed with a great dread of the dangers which they think it must involve".

Attention may also be drawn to a review of a French monograph by Paul Gingeot, entitled "Essai sur l'Emploi thérapeutique de l'Alcool chez les Enfants, et en général sur le Rôle de cet Agent dans le Traitement des Maladies aiguës fébriles", 1867, since our views on this subject have meanwhile so radically changed: "This book is an interesting specimen of a movement which has been going on during the last few years in France, and will certainly have important results on the treatment of disease . . . With a courage which at first found few imitators, M. Béhier threw aside

THE RECOGNITION AND MANAGEMENT OF PSYCHIATRIC DISORDERS IN THE FIELD OF GENERAL MEDICINE

By IAN SKOTTOWE, M.D., D.P.M.

Physician Superintendent, Bucks County Mental Hospital; Physician in Charge, Department of Nervous and Mental Diseases, Royal Bucks Hospital.

A PSYCHIATRIC case is one in which some change or defect in the patient's personality is a cause or a symptom of an illness; but a knowledge of psychiatric principles is relevant to the management of many other illnesses in which there is a need to deal with the patient as a person. In any illness, the causes, symptoms or treatment may lie mainly in the bodily, the personal or the social sphere. The causes may arise in one of these spheres, the symptoms appear in another; whilst therapeutic activity may be needed in all or any of them. The main types of these relationships may be grouped as follows :—

(1) *Symptomatic mental illness.*—It is intelligible that brain disease, toxæmia or malnutrition may so influence functions such as perceiving, remembering, reasoning and controlling of emotions, that personal, or psychological, symptoms result; such symptoms may have social consequences varying from occupational inefficiency to grossly aberrant conduct. The remedial treatment of a disorder so produced lies essentially in the field of general medicine, although treatment may well be necessary, not only as a direct attack upon the underlying causal bodily disorder but also in the psychological sphere, by explanation, reassurance and occupation, and in the social sphere by the rearrangement of the patient's way of living at work or at home.

Apart from true symptomatic mental disorders, there may be an indirect causal relationship between bodily disorder and personality change. Serious illness, uncomplicated pregnancy or operation, for instance, may, as mental experiences, induce morbid states of anxiety, depression, excitement or suspiciousness in personalities that have proclivities towards such responses without necessarily implying an intervening stage of cerebral dysfunction; whilst physical deformity or maiming may similarly produce enduring changes in the personality and general outlook on life.

(2) *Psychosomatic disorders.*—It is now known that not only intense, brief emotions but also enduring emotional attitudes may influence bodily functions; they do so in different ways, and do not produce just a crude undifferentiated somatic response, intelligible only as adrenal-sympathetic hyperactivity. The cause-effect relationship between the personality and the organs is a two-way traffic. And in so far as personal experiences and attitudes are evoked by social events, not only is there a series of socio-

were blood-letting, in this day, an unknown remedy, and were some man to discover it, we should receive that man as of the greatest amongst us, and send him to posterity as one of the lights of the age".

In the December issue a paper by the Editor, Dr. Anstie, may be noted: "On Muriate of Ammonia as a Remedy for Some Nervous Disorders": "Muriate of ammonia is one of those commonplace and unattractive substances which we, in this country, are little apt to credit with extensive remedial properties in disease . . . Few agents in the whole Pharmacopœia have more decided and reliable therapeutic properties. The apathy with which its pretensions are treated in England, contrast singularly with the wide and varied uses to which it has been applied by German physicians, whose faith in its powers, to say the truth, seem to me to run into the other extreme of excess". Doubtless, few people to-day are acquainted with the medicinal virtues of the drug which "appears, in fact, when given in therapeutic doses, to be a pure tonic stimulant to sensitive nerves, raising them to a level of tense vitality *too high* for the explosive perturbations which, when carried to the brain, are translated as *pain*, and to the vaso-motor system, directly inciting to a superior tone of the systemic vessels, which puts an end to that exaggerated passive congestion of viscera which is known to be fatal to the healthy performance of the function of secretion". How elegant this sounds, but, to the modern ear, what unscientific jargon!

In the same number a case is reported from the *British Medical Journal*: "Diabetes Cured by the Administration of Peroxide of Hydrogen". Treatment began with $\frac{1}{2}$ -drachm doses of the ethereal essence, gradually increased to a drachm three times a day. The doctor at the same time also materially relaxed the rigidity of the patient's diet, and "discontinued much that was disagreeable and objectionable for one more consonant to his taste and appetite". After ten weeks' steady perseverance, with occasional fluctuation, the patient recovered.

Eighty years ago many subjects in medicine were still enveloped in mystery and superstition. The scientific era of the infectious diseases was still far ahead. Thirty-seven years had to elapse before the organism of syphilis was discovered, and still another two years after that before the introduction of the Wassermann test. Malaria was still a disease full of mediæval theories and speculations. The word *bacteriology* was as yet unknown. In 1887, E. M. Crookshank was appointed to the Chair of Bacteriology at King's College—the first chair in this country. The Pasteur Institute was founded in the following year. Lister's following was still small. X-rays were still awaiting their accidental discovery. No one had heard of vitamins. There was no such thing as endocrinology. At that time, the thyroid, for example, was looked upon as a mere vestige, as was the pituitary body. Another eight years had to pass before Cesare Lombroso's "*L'Uomo delinquente*" stimulated the study of insanity and influenced the administration of prisons and mental hospitals.

udely assessed, are two of the most important factors in determining the degree of insight that the patient can be persuaded to have into the way in which his symptoms have been produced; and also the extent to which he can be taught to deal with himself and his situations, and so learn to make his own decisions and stand on his own feet.

It may therefore be seen that just as there was, and is, a need to bring general medicine into psychiatry, so there is a need to bring psychiatry into general medicine. Whether one practices medicine as a physician for internal disorders, as a psychiatrist, or as the medical sociologist of modern times, one must have a comprehensive outlook and some knowledge of the other man's field of activities. Each doctor should be at once a strategist and a tactician—a strategist in so far as he must conceive the grand plan, the field in which action is necessary; a tactician in so far as he is a specialist whose business it is to carry out the detailed technical procedures of that action.

Incidence expectation.—In summary, the work of Whitby, Pearson and Collier shows that the expectation of psychiatric disorders in general medicine is, so far as neuroses go, about 10 per cent. of patients seen in general practice, 16 per cent. of general hospital out-patients, and about 30 per cent. of protracted disabilities of all kinds, peak figures being recorded in cases which present gastric or abdominal, and to a lesser extent, cardiac symptoms. More than half of these cases will be anxiety states, many of them with accompanying bodily symptoms; about a third will be mild depressive illnesses; up to a tenth will have hysterical disabilities.

The more serious psychotic disorders have an annual new case incidence of about 1 per 1000 of population and are not likely to produce more than three or four cases a year among the patients who are seen in the average practitioner's professional activities. In practice, they are distinguished, though not very sharply, by their severity, by the fact that the patient no longer speaks the same language, harbours manifest delusions, is under some over-mastering emotional disturbance or is grossly disordered in his intellectual functions or in his conduct. Notwithstanding the severity of these illnesses, the patients still have, in the mass, an "odds-on" chance of satisfactory readjustment.

CRITERIA OF RECOGNITION OF PSYCHIATRIC DISORDERS

(1) *In the patient's complaint.*—For present purposes, the relatively rare examples of gross illness in which the patient does not complain or recognize that he is ill, although this may be obvious to others from the expressions of delusions, conduct disorder and so on, need not be considered. The great majority of patients come willingly—some almost too eagerly—to the doctor. The patient may complain of psychological symptoms, such as "nerves", depression, feeling of being "in a dream", lack of confidence, loss of interest, inability to concentrate, and so on; or he may not refer at all to symptoms at the personal level, but may direct attention exclusively to symptoms such as breathlessness, palpitation, sweating, weak legs, diarrhœa,

somatic influences as seen in industrial diseases, housing relevant to tuberculosis, and so on; there is also a series of socio-psychosomatic influences, of which gastric disorders in psychologically similar but technically diverse occupations, or hypertension in exasperated executives, or even troublesome palmar hyperhidrosis in anxious surgeons (itself a miniature vicious circle) may be regarded as examples. There are many others, notably a large group of visceral spastic disorders, including asthma and spastic colon, disturbances of cardiac rhythm, dyspnoea, effort syndrome, vertigo, angioneurotic oedema, glycosuria, and so on. Such conditions are true psychosomatic disorders. Their essential feature is the direct production of somatic symptoms by the influence of personal experiences upon visceral, vascular and muscular functions through efferent neural pathways, with or without adrenal or other endocrine mechanisms intervening. In many such disorders the syndrome is aggravated by the fact that the patient experiences centripetal nervous impulses arising from the over-responsive viscera. Often so much so, that the accent in symptomatology is on the somatic state, sometimes to the exclusion of the underlying personal, psychological or situational cause, which must therefore be sought by a methodically conducted psychiatric interview, if the illness is to be rendered intelligible and treated rationally. So far as is known it is in terms of thalamic, hypothalamic and autonomic functions that further elucidation of the means by which these effects are produced by primarily social and psychological causes may be looked for; but we still have to recognize and deal with those causes in terms of personal experiences.

(3) *Motivated disability*.—Apart from true psychosomatic disorders, there are other less direct interrelationships between the patient as a person, on the one hand, and the functions or dysfunctions of his organs on the other. Illness, originally somatic, may merge into a disability that continues long after the somatic condition has healed, because it serves as an escape from a situation that is distasteful to him in degrees varying from mere uncongeniality to repellant intolerance. The degree of repugnance that the situation is likely to evoke must be assessed against the toughness or morale of the patient. The essential quality of disability arising or prolonged in this way is that the patient has a motive for being, or continuing to be, ill. He may be aware of this to an extent that varies from clear consciousness of it (practically malingering) to apparently no awareness at all (one form of hysteria). Such disability may be complicated by, or it may complicate, the true psychosomatic disorders already described. Either may occur in a personality that is well, or poorly, endowed intellectually; although the true psychosomatic illnesses tend to be linked with the better endowed personalities, and the motivated or hysterical types of disability with the less well endowed. Intellectual endowment as evidenced by scholastic occupational attainment, by test procedures and by the presence of "nous" or common sense, together with the endowment of moral fibre or "guts" which cannot be measured numerically, although its presence or absence can be

crudely assessed, are two of the most important factors in determining the degree of insight that the patient can be persuaded to have into the way in which his symptoms have been produced; and also the extent to which he can be taught to deal with himself and his situations, and so learn to make his own decisions and stand on his own feet.

It may therefore be seen that just as there was, and is, a need to bring general medicine into psychiatry, so there is a need to bring psychiatry into general medicine. Whether one practices medicine as a physician for internal disorders, as a psychiatrist, or as the medical sociologist of modern times, one must have a comprehensive outlook and some knowledge of the other man's field of activities. Each doctor should be at once a strategist and a tactician—a strategist in so far as he must conceive the grand plan, the field in which action is necessary; a tactician in so far as he is a specialist whose business it is to carry out the detailed technical procedures of that action.

Incidence expectation.—In summary, the work of Whitby, Pearson and Collier shows that the expectation of psychiatric disorders in general medicine is, so far as neuroses go, about 10 per cent. of patients seen in general practice, 16 per cent. of general hospital out-patients, and about 30 per cent. of protracted disabilities of all kinds, peak figures being recorded in cases which present gastric or abdominal, and to a lesser extent, cardiac symptoms. More than half of these cases will be anxiety states, many of them with accompanying bodily symptoms; about a third will be mild depressive illnesses; up to a tenth will have hysterical disabilities.

The more serious psychotic disorders have an annual new case incidence of about 1 per 1000 of population and are not likely to produce more than three or four cases a year among the patients who are seen in the average practitioner's professional activities. In practice, they are distinguished, though not very sharply, by their severity, by the fact that the patient no longer speaks the same language, harbours manifest delusions, is under some over-mastering emotional disturbance or is grossly disordered in his intellectual functions or in his conduct. Notwithstanding the severity of these illnesses, the patients still have, in the mass, an "odds-on" chance of satisfactory readjustment.

CRITERIA OF RECOGNITION OF PSYCHIATRIC DISORDERS

(1) *In the patient's complaint.*—For present purposes, the relatively rare examples of gross illness in which the patient does not complain or recognize that he is ill, although this may be obvious to others from the expressions of delusions, conduct disorder and so on, need not be considered. The great majority of patients come willingly—some almost too eagerly—to the doctor. The patient may complain of psychological symptoms, such as "nerves", depression, feeling of being "in a dream", lack of confidence, loss of interest, inability to concentrate, and so on; or he may not refer at all to symptoms at the personal level, but may direct attention exclusively to symptoms such as breathlessness, palpitation, sweating, weak legs, diarrhoea,

indigestion, headache; or he may produce symptoms not clearly classified as psychological or somatic; for instance, insomnia, a feeling of unsteadiness, or of floating in space. First it should be ascertained whether or not the symptoms are in the main inherently psychological. Such a complaint might be, for instance: "My mind is blank; I can't remember anything"—when it is obvious that the patient is in fact thinking quite actively and has no gross impairment of memory. Or it might be: "I just feel hopeless, life isn't worth living, I feel I've made a mess of everything". The interrogative complaint, especially if it is quaint, is peculiarly suggestive of a psychiatric disorder: "Why do I get this burning heat?" "What is it makes the back of my head open and shut?" "Is it just the nerves?"—always in a peevish tone, often with an uneasy smile, and frequently followed by a request for confirmation addressed by the patient to an accompanying relative. A careful scrutiny of the quality of the symptoms and the setting in which they occur will often give a clear indication of the field in which the prepotent causes lie. A garrulous patient who complains of headache, for example, and says on inquiry, that "it's not exactly a pain, it's my thoughts that keep going round and round just here, it keeps me awake at night", is *prima facie* most unlikely to have an intracranial space-occupying lesion. A complaint of palpitation, breathlessness, weakness of the legs, "everything going dim", and an impending swoon, that is experienced paroxysmally by a young woman when she is walking down the hill past her faithless fiancé's house is unlikely to betoken mitral stenosis or disseminated sclerosis, although it does not dispel the need for careful cardiac and neurological examination, not only because such an examination is an essential to reassure the patient, but because every now and again you will find a young woman who *has* mitral stenosis, or disseminated sclerosis, as well as a faithless fiancé; and occasionally you will find one in whom the result of a Friedman test—positive or negative as the case may be—is the most important single fact in rendering the illness intelligible. For these reasons, apart from any others, the somatic side of the examination should never be approached with a preconception that it need only be cursory.

(2) *In the biography of the patient.*—The patient's complaint leads naturally to history taking. In a psychiatric case it is not only the history of an illness, it is also the biography of a person that is important. The act of obtaining this constitutes a major part of the initial psychiatric interview. In the course of it a general assessment of the patient's mental state should be made systematically under the five main aspects of mental activity, namely, *behaviour, talk, mood, the content and trend of thought, and the state of the perceptual sensorial intellectual functions* (orientation, memory, grasp of current events, judgment and foresight). Starting traditionally from the point when the patient was last quite well, proceed with the history of the immediate attack of illness, the quality, setting and variations of the symptoms; and note especially when the patient stopped work. A patient who has been off work for three months without a somatic diagnosis being

apparent on examination, or, more still, one who in the last year has had three months' sick absence in broken periods of one or two weeks at a time, is extremely likely to be a psychiatric case, even if his complaint be exclusively somatic. In clinical psychiatry, dates matter more than doctrines.

Next, inquire for previous attacks of the same kind of illness, even if of less intense degree. Their presence fortifies a psychiatric diagnosis. Then detail other illnesses, accidents, hospital admissions. Look out for the accident-prone. The man who has been on Workman's Compensation three times in as many years (usually revealed with reluctance) is as bad a psychiatric risk as he is an insurance risk.

From the mainly medical, the examination passes to the purely personal. Where was the patient born and bred? What did his father do? How many brothers and sisters has he, and where does he come in? Have any of them had any nervous illness? (The very common anxiety and depressive states follow mainly a dominant pattern of inheritance, shown clinically by their presence in one parent and half of the siblings.) Where did the patient go to school? Age of leaving? Attainments in work and play? Any excessive difficulties about puberty? What is his occupational record, and how do he and his job—and his associates—fit one another? Marriage? Special experiences? Attitude to major common topics of life (for example, religion, sex) and general cultural background and outlook? Alteration of habits in, for instance, alcoholic consumption, smoking, hobbies and interests, religious observance? Such a biography will give a sound indication of the kind of person the patient is, of what general and special problems and experiences have troubled him and of how he has dealt with them and been moulded by them. From this it can be seen whether or not he has proclivities towards psychiatric illness, and some assessment can be made of the respective influences of nature and nurture.

(3) *In the examination of the patient.*—In the course of the foregoing interview, of which the salient findings should be discussed and checked with a relative, always with due regard to confidential matters, much of the mental examination will have been made. It remains to decide whether special further examination of the mental state is required or not. It is always important to assess the presence or absence of clouding of the intellectual functions, and if this is not already obvious, simple calculations, absurdities and retention tests can be applied easily and acceptably at an appropriate point in the interview, provided they are moulded to the patient's occupational, educational and cultural status. The presence of clouding, or of impaired test performance, strongly suggests the presence of an organic causal factor, which may vary from mere fatigue to gross brain disease. In young people with a poor scholastic and occupational record, concealed mental defect may be revealed—and in any event a helpful rough assessment of intellectual capacity obtained—by a simple standardized verbal or reading test and a non-verbal test such as the "Porteous mazes", as incorporated in Burt's (1933) "Handbook of Tests". These take only a

few minutes to apply, and if they produce significant findings, fuller testing, without consuming the practitioner's time, may be done by using self-administering verbal and non-verbal tests, such as the "Penrose-Raven matrices" (1938) and the "Mill Hill vocabulary test" (1943). I see no objection to these admittedly special, but essentially simple, procedures being undertaken aside from the field of specialized psychiatry, provided that they are used only as a general guide, in confirmation of the biography, and that no attempt is made at more recondite interpretations of anomalous results (for example scattering or discrepancy) which should indicate the need for specialized psychiatric review. The results, considered against the biography, may be particularly helpful in revealing the core of the problem and saving time in much valueless psychological exploration in patients who have bitten off more than they can chew occupationally or, on the contrary, are suffering from monotony and boredom at work because it is too limited for their capabilities. In either event, secondary anxiety with or without somatic symptoms may be quite intractable until occupational reselection has been accomplished.

The physical examination should be carried out thoroughly and in such a way as to convince the patient that nothing is being overlooked. Sometimes the very nature of a somatic symptom, just as the nature of a psychological symptom, indicates the probable field of its origin. This is well seen in the respective distribution of hysterical and other distributions of anæsthesia, and in some forms of motor disorder. Investigations beyond ordinary clinical examination should be done only if they are indicated by that examination. Over-investigation may aggravate the symptoms; and yielding to the patient's demands for investigation that *he* thinks are necessary, but are not indicated by the general clinical picture, is seldom justified; partly because such a procedure fortifies him in an erroneous conception of the nature of his illness; partly because to accede to it tends to suggest that the practitioner has little confidence in his own clinical methods, or that the whole illness is so mysterious and unique that it can be unravelled only by means of impressive apparatus or rituals directed towards the body rather than by commonsense appraisalment of the facts of a personal situation. In any event, if a symptom is psychogenically produced, no amount of somatic investigation will, by itself, remove it. I have never seen, for instance, a syphilophobia banished by the assurance of repeated negative Wassermann reactions. That, however, is no reason for not doing a Wassermann in the case of a patient who has run the risk of syphilis, whether or not he fears it. Some investigations, for instance, lumbar puncture in some early organic psychoses; a barium swallow in apparent nervous dysphagia; or chest X-ray, sedimentation rate and other blood examination in cases with asthenia and loss of weight as presenting symptoms, can seldom be avoided with safety. Serious organic disorders and psychological abnormality may coexist without at first being very intimately related to one another. A neurotic middle-aged patient is no less prone to the diseases of middle age than anyone else.

He may have anæmia as well as anxiety; cancer as well as a phobia. In psychiatry, of all aspects of medicine, there is the greatest need for vigilant clinical observation and sound conclusions based on thorough examination.

THE PRINCIPLES OF MANAGEMENT

(1) *Personal*.—Most psychiatric patients feel that they are misunderstood and are different from everyone else, and may feel that they are unwanted and have not had a fair deal. When they come into medical hands they are tired of being told that there is nothing wrong with them, that it is just imagination or nerves and they should pull themselves together. On the other hand a few, who really have very little wrong with them, are convinced that they are seriously ill, paralysed, nearly blind or whatever it may be, largely through faulty handling, usually, but not invariably, by relatives. In either event, the patient appears as the centre-piece of a family situation in which tempers have been frayed, work lost, holidays postponed; he is near to being regarded as a nuisance or an interesting invalid, ripe for life-long suffering, as the case may be. The very essence of good management is first that the practitioner should make up his own mind about how the symptoms have been produced; second, that he should formulate his findings in a way that is convincing to the patient and intelligible to the relatives; and third that he should point out the lines on which remedial action can be taken. All this takes time; but in my experience it is better, whenever possible, to make the initial interview and examination a thorough and decisive affair. This may take anything from a half to one-and-a-half hours—the average is about three quarters—but it greatly diminishes the frequency and length of subsequent interviews, and it is therapeutically much more effective than repeated brief placations and piecemeal investigations spread over weeks or months, accompanied by persistent disability and uncertainty.

Treatment has a meagre chance of success if there is continuous evasive action behind a screen of multiform investigations and a succession of “no evidences”. The “functional-organic” conception is of little use as a basis on which to diagnose or manage these cases. Distress is distress, whether it arises from angina pectoris or from an absconding spouse. It is no use telling a patient with palpitation that there is nothing wrong with his heart unless you also tell him wherein you think there *is* something wrong; he will still have his palpitation, and he just won’t believe you.

When the nature of the illness has been formulated, an attempt should be made to get the patient to see clearly the situation in which he is, to understand what his problem is and to reduce it, if possible, to a simple choice of alternatives; it is for the patient alone to decide which of them he will choose. Great care should be taken neither to judge nor advise in the moral sphere; but it is quite in order to offer an opinion as to the probable medical effects upon the patient of one choice or the other.

(2) *Medicinal*.—When the psychological side of the illness has been dealt

with, attention should be directed to the question of symptomatic relief by medicinal means. The patient needs not only insight and encouragement; he needs also a good sleep, adequate nutrition, the easement of excessive visceral responsiveness and attention to hygiene generally. Technical details need not be considered here; but the purpose of any therapeutic measures of this kind should be explained and the patient should not be allowed to look on them as substitutes for readjusting his outlook and activities.

(3) *Social*.—There remains the question of social measures that may be necessary. Broadly, are there factors at home or at work that are both relevant and remediable? If so, it is essential to try to remedy them either by interviewing relatives, and making recommendations about alternative employment, or by sending a trained psychiatric social worker to do so. It may be imperative to get the patient right away from his customary environment for a time. In most cases it is worth while waiting for a week or two in order to see what influence a properly conducted psychiatric interview and appropriate medicinal treatment will have, but in some it will be evident from the start that the patient must be got away. If the illness is of recent onset, and if exhaustion, anorexia and insomnia are prominent, in short if the case is likely to benefit from brief intensive physical treatment, such as continuous narcosis or modified insulin coma, then admission to the psychiatric department of a general hospital is indicated, especially if the initial examination has shown that further investigation of the somatic state or physical treatment of psychosomatic symptoms is essential. In other cases, in which the need for environmental change together with extended and repeated psychiatric interviews is indicated, admission to a neurosis centre is appropriate, especially if treatment is likely to be needed for a rather longer period and must include a certain amount of re-education in a way of living and in occupational restoration.

In a very small proportion of cases, the need for mental hospital admission, on the criteria described, will be apparent. In such cases the patient should always be offered the opportunity of voluntary admission—there is at least an even chance that he will accept it. In all these instances of proposed admission it is most important to do something to ensure that things—and people—at home will be looked after while the patient is away and to convince him or her of this—yet another function of the social worker. Finally, it must not be thought that a high proportion of psychiatric cases need in-patient treatment. Scrutiny of my own out-patient figures suggests that not more than 15 to 20 per cent. of them will need it, whether in general hospital, neurosis centre or mental hospital. The great majority can be satisfactorily treated without admission; and in about half of them this is achieved principally, if not exclusively, by means of a properly conducted, patient and thorough initial interview and examination without the need for any highly specialized technical procedures; whilst in most of the remainder it is still, in my experience, the proper handling of the initial interview that is the most important single event in the management of the case.

RESIDUAL DILATATION OF THE UPPER URINARY TRACT FOLLOWING PREGNANCY

By R. E. NORRISH, F.R.C.S.

Consulting Surgeon, City General Hospital, Stoke-on-Trent.

FOR many years it has been known that changes occur in the form of the renal pelvis and ureter during pregnancy, and the condition has been widely recognized and described. The expansion which takes place has been stated to be an accompaniment of the gravid state in more than 80 per cent. of women (Trant and McLane, 1937), and gradually proceeds from the early weeks, throughout pregnancy to term, thereafter receding in the uncomplicated case to approximate normality.

CAUSAL FACTORS

The causes of these changes have been widely debated, and the problem is still by no means settled. It was at first believed that pressure of the enlarging uterus upon the ureter at the brim of the pelvis was the underlying cause of the dilatation; but it has been shown that the process may begin before the uterus has reached the brim, and this is illustrated by the fourth case recorded here. The view that the hormonal action of progesterone is the responsible agent has strong support, the relaxation of the uterine muscle brought about by this substance during the course of pregnancy being reflected in the atonic expansion of the plain muscle of the urinary tract, and this includes the bladder (Langworthy and Brack, 1939), as well as the ureters and pelves. Not only is there a widening of the ureter, but also an increase in its length, as is so often seen by the twists and kinks in pyelographic studies. These changes have been produced by the administration of progesterone in large doses to non-pregnant women (Hundley, Diehl and Diggs, 1943).

The absence of a preliminary hypertrophy of the ureteric muscle, the diminution in peristaltic activity, and the fact that the minor calyces maintain their normal cupping, are against the theory of a rise of tension in the uretero-pelvic system, such as might be produced by simple pressure effect. That pressure, however, may play a part is certain, and this not only in the later stages, for the dilatation may sometimes be present on one side only, and at a comparatively early stage, as in the second case described, the opposite side remaining normal and contractile. Further, the expansion is fairly uniformly confined to the abdominal course of the ureter, the pelvic segment remaining within more normal limits.

Whatever the precise combination of causes, a flaccid, dilated, and atonic

system is associated with a urinary stasis and a predisposition to urinary infection; the frequent occurrence of pyelitis in pregnancy is one of the results.

Reversion to normal form, with the return of full tone to ureter and bladder, occurs in the uncomplicated case by the sixth week following delivery (Trant, McLane and Kuder, 1939), but this may be considerably delayed by the incidence of infection; the prolonging of this may result in a variable degree of permanency of the expansion. Such residual dilatation may be further consolidated by subsequent pregnancies until the child-bearing period is passed, leaving finally an atonic pelvis and ureter stiffened by fibrosis and lacking all power to contract. The accompanying pyelograms are presented as illustrative of this etiological background in many patients with chronic urinary infection.

ILLUSTRATIVE CASES

Case 1. Normal pregnancy dilatation, with recession after delivery.—A patient aged twenty-three years, primigravida, at the 34th week. The first pyelogram shows a typical enlargement of the left urinary tract, the right giving a faint shadow of a wide dilatation. The second pyelogram, eight weeks after delivery, indicates a recession on both sides to normal dimensions. She suffered a transient urinary infection, which cleared up after delivery.

Case 2. Unilateral pregnancy dilatation.—A patient of thirty-one years had had four previous pregnancies, unassociated with urinary infection. She was admitted to hospital at the 14th week with pain in the right loin, and a normal, sterile urine. Her pyelogram showed a dilatation of the right ureter in its abdominal course, and of the pelvis above it. Her symptoms subsided, and her urine remained clear.

Case 3. Residual dilatation of the right upper urinary tract in a patient past the childbearing age.—This patient was aged fifty-two years and had had six children. With her first pregnancy she had had pyelitis and this had recurred throughout her subsequent pregnancies. For many years afterwards she suffered from backache, dysuria, and increase of frequency. There was tenderness in her loins, and coliform infection of her urine. Intravenous pyelography revealed an expanded and elongated right ureter and pelvis, with kinking and twisting of the former—a replica of the form familiar in the pregnancies of younger women.

Case 4. Dilatation of pregnancy superimposed upon a previous residual expansion, with partial recession following delivery.—A patient of twenty-five years, who had had two previous pregnancies. During her first, four years before, she suffered from pyelitis and hæmaturia, and the infection had persisted intermittently since. An exacerbation of this, with dysuria and backache, brought her to hospital, and intravenous pyelography showed a much dilated right renal pelvis and ureter, the left being normal. Her urine was infected and contained pus. Three months later she became pregnant, and at 2½ months her pyelogram showed wide dilatation of both sides; at 4½ and 6½ months the condition was the same. Her pregnancy terminated normally. Four months after delivery her pyelogram showed recession of her left side to normal, but in the right her previous degree of dilatation persisted. She still had her urinary infection.

References

- Hundley, J. M., Diehl, W. K., and Diggs, E. S. (1943): *Amer. J. Obstet. Gynec.*, **48**, 858.
 Langworthy, O. R., and Brack, C. B. (1939): *Ibid.*, **37**, 121.
 Trant, H. F., and McLane, C. M. (1937): *Surg. Gynec. Obstet.*, **64**, 51.
 —, —, and Kuder, A. (1939): *Int. Abstr. Surg.*, **67**, 568.



CASE 1a — Normal pregnancy dilatation



CASE 1b — Recession to normal two months after delivery



CASE 2 — Unilateral pregnancy dilatation



CASE 3 — Residual pregnancy dilatation persisting in a patient past the child-bearing age (52 years)

system is associated with a urinary stasis and a predisposition to urinary infection; the frequent occurrence of pyelitis in pregnancy is one of the results.

Reversion to normal form, with the return of full tone to ureter and bladder, occurs in the uncomplicated case by the sixth week following delivery (Trant, McLane and Kuder, 1939), but this may be considerably delayed by the incidence of infection; the prolonging of this may result in a variable degree of permanency of the expansion. Such residual dilatation may be further consolidated by subsequent pregnancies until the child-bearing period is passed, leaving finally an atonic pelvis and ureter stiffened by fibrosis and lacking all power to contract. The accompanying pyelograms are presented as illustrative of this etiological background in many patients with chronic urinary infection.

ILLUSTRATIVE CASES

Case 1. Normal pregnancy dilatation, with recession after delivery.—A patient aged twenty-three years, primigravida, at the 34th week. The first pyelogram shows a typical enlargement of the left urinary tract, the right giving a faint shadow of a wide dilatation. The second pyelogram, eight weeks after delivery, indicates a recession on both sides to normal dimensions. She suffered a transient urinary infection, which cleared up after delivery.

Case 2. Unilateral pregnancy dilatation.—A patient of thirty-one years had had four previous pregnancies, unassociated with urinary infection. She was admitted to hospital at the 14th week with pain in the right loin, and a normal, sterile urine. Her pyelogram showed a dilatation of the right ureter in its abdominal course, and of the pelvis above it. Her symptoms subsided, and her urine remained clear.

Case 3. Residual dilatation of the right upper urinary tract in a patient past the childbearing age.—This patient was aged fifty-two years and had had six children. With her first pregnancy she had had pyelitis and this had recurred throughout her subsequent pregnancies. For many years afterwards she suffered from backache, dysuria, and increase of frequency. There was tenderness in her loins, and coliform infection of her urine. Intravenous pyelography revealed an expanded and elongated right ureter and pelvis, with kinking and twisting of the former—a replica of the form familiar in the pregnancies of younger women.

Case 4. Dilatation of pregnancy superimposed upon a previous residual expansion, with partial recession following delivery.—A patient of twenty-five years, who had had two previous pregnancies. During her first, four years before, she suffered from pyelitis and hæmaturia, and the infection had persisted intermittently since. An exacerbation of this, with dysuria and backache, brought her to hospital, and intravenous pyelography showed a much dilated right renal pelvis and ureter, the left being normal. Her urine was infected and contained pus. Three months later she became pregnant, and at 2½ months her pyelogram showed wide dilatation of both sides; at 4½ and 6½ months the condition was the same. Her pregnancy terminated normally. Four months after delivery her pyelogram showed recession of her left side to normal, but in the right her previous degree of dilatation persisted. She still had her urinary infection.

References

- Hundley, J. M., Diehl, W. K., and Diggs, E. S. (1943): *Amer. J. Obstet. Gynec.*, 48, 858.
 Langworthy, O. R., and Brack, C. B. (1939): *Ibid.*, 37, 121.
 Trant, H. F., and McLane, C. M. (1937): *Surg. Gynec. Obstet.*, 64, 51.
 —, —, and Kuder, A. (1939): *Int. Abstr. Surg.*, 67, 568.

SUNBURN: PREVENTION AND TREATMENT

By E. W. PROSSER THOMAS, M.D.

Physician, Skin Department, National Temperance Hospital, London.

SUNBURN may vary from a simple erythema with moderate discomfort to an extensive vesicular erysipelas-like eruption associated with pain, swelling, chills, fever, and shock. Sunlight is a "primary" skin irritant in the sense that it will produce an inflammatory reaction in the majority of persons if dosage is excessive. The adverse effects of strong sunlight are not due to the heat rays of the solar spectrum but to the actinic rays—the invisible rays beyond the violet; thus extreme degrees of solar dermatitis may be caused by cold light when its intensity has been increased by reflection from ice, snow or water. Heating the skin before exposure, however, accentuates cutaneous susceptibility to actinic light.

Strictly speaking, sunburn is a photochemical reaction to ultra-violet energy in the spectral range 2,900 to 3,200 Å., and is characterized by local erythema which is followed, with heavy doses, by œdema and erythematous flare, and later by desquamation, pigment formation, and darkening of existing pigment. Many factors determine the degree of reaction, among them being duration and intensity of exposure, individual susceptibility and that of the particular area exposed, the thickness of the horny layer, and the amount of pigment in the skin. Blondes and persons with delicate skins which pigment feebly are more susceptible, although the natural protective mechanism depends less upon pigment formation than upon the thickness of the corneum, which acts as an absorbing and scattering barrier against the burn-producing rays. Sweat provides some protection. The skin varies much in sensitiveness to sunlight in different parts of the body; parts habitually exposed are considerably less sensitive than those normally covered. The most vulnerable areas are the inner aspect of the arms and thighs, the popliteal fossæ, the sides of the chest, and the back. Endocrine function appears to play a part by influencing cornification and pigmentation; thus sunburn is said to occur more readily on the first day of the menstrual cycle and between the second and the seventh month of pregnancy.

Clinically, an acute solar dermatitis develops after a latent period varying from thirty minutes to six hours, with erythema accompanied by itching and burning in the exposed areas. In more severe cases the reaction proceeds to actual inflammation and the formation of vesicles or even of large bullæ. Œdema may be so gross as to close up the eyes when the face is involved. Conjunctivitis may occur. When the dermatitis subsides the epidermis peels in large shreds leaving a variable degree of pigmentation. The affected areas after desquamation are always more sensitive. Severe



1—Residual dilation of the right side from previous pregnancy



CASE 4b.—Additional dilatation superimposed on her residual expansion by a fresh pregnancy. Pvelogram at 24 months



CASE 4c —Residual dilatation again persisting four

Regarding *selective chemical protectives*, it has been shown that *p*-aminobenzoic acid has an absorption band in the ultra-violet spectrum which embraces all the "sunburn rays". The pure substance is said to be non-toxic and non-irritating to human skin, and does not soil the clothing. It is easily miscible with greasy bases, cold creams and emulsion bases. The sunburn-protecting action of *p*-aminobenzoic acid has been investigated by Rothman and Henningsen (1947), who regard it as effective even against extremely strong ultra-violet irradiation, such as occurs on glaciers or on the ocean. They recommend 15 per cent. *p*-aminobenzoic acid in a vanishing cream base. Alternatively, 10 per cent. *p*-aminobenzoic acid in 70 per cent. industrial spirit may be used. A powdery white film is left on the skin when the alcohol evaporates and should be rubbed into the skin until the powder disappears. These preparations should be re-applied after swimming and after every two or three hours of exposure. Slight tanning of the skin may occur. Solar urticaria and the darkening of freckles cannot be prevented by *p*-aminobenzoic acid ointments and lotions.

Many vegetable oils possess some screening action of their own without the addition of sun-screen chemicals; of these, sesame oil seems to be the most effective. Mineral oils are of no use in this respect. The application of a vegetable oil before exposure is also useful in keeping the skin supple against the drying effects of the sun and wind. The intense pigmentation which follows lasts well because desquamation is avoided. The following is a sample formula for a "suntan" oil:—

Methyl salicylate	10 per cent.
Sesame oil	50 per cent.
Liquid paraffin	40 per cent.

TREATMENT OF ACUTE SUNBURN

The first care in local treatment must be not to add insult to injury by using any form of strong application, especially antiseptics, to the burned areas. Analgesic ointments and proprietary "balms" are also best avoided, for they may contain skin irritants such as camphor or menthol. The skin requires only soothing applications, such as simple calamine lotion (either aqueous or oily), or moist compresses of 1 per cent. aluminium acetate solution or weak lead lotion. Wet dressings and evaporating lotions, however, should not be applied to extensive areas because of the risk of chilling. The areas should be cleansed gently with arachis oil or liquid paraffin and not with soap or water.

To counter secondary infection, the skin may be mopped daily with a solution of mercury perchloride, 1:4000; blisters should be snipped and painted with aqueous crystal violet, 1 per cent., or the whole area may be sponged thinly with crystal violet, $\frac{1}{2}$ per cent. in calamine lotion. One of the antihistamine agents should be given by mouth, for example, antistin, 100 mgm. three times a day, until itching has ceased and the skin is quiet.

sunburn is associated with symptoms of shock.

Apart from common *complications* such as impetigo and folliculitis due to secondary pyogenic infection, sunburn may be the precursor of herpes simplex, vitiligo, telangiectasia, or lupus erythematosus. The primary solar dermatitis may determine photosensitization, so that attacks of actinic dermatitis may follow minimal exposure in the future.

Chronic sunburn.—Persons who are habitually exposed to strong clear sunlight, such as sailors and farmers, especially in Australia, may develop skin changes which are so pronounced as to resemble radio-dermatitis. These consist of atrophy, wrinkling, pigmentation and de-pigmentation, telangiectases and, particularly, of small warty excrescences (solar keratoses), which are very liable to undergo malignant change into basal or squamous-cell carcinoma.

PREVENTION

Persons with susceptible skins, especially if they are unaccustomed to the open air, should keep out of strong direct sunlight and should live within the limits of their sun tolerance. The best colours for protective garments are brown or khaki, orange and red; white is the least effective. The protective value of all fabrics is greatly reduced when they are wet.

During the war various substances were tested for their efficacy as protectives against sunburn in exposed sailors and airmen. For instance, Lukiesh *et al.* (1946), working for the U.S.A. Air Forces, sought a preparation which was stable over a wide range of temperatures, non-toxic, readily available, and not easily washed off the skin. They found that dark red veterinary petrolatum gave almost complete protection and was satisfactory in every other respect. But there are obvious disadvantages to the use of this substance in civilian practice.

The usual prophylactics are based on the fact that skin pigmentation is increased by rays of wave-lengths different from those which produce erythema; hence *suntan*, which many people desire, can be induced without preliminary *sunburn*. Thus protectives are of two kinds, namely, (a) "sunshade" preparations, which screen the skin against the pigmenting as well as the burn-producing rays, and (b) "suntan" applications, which filter out the sunburn rays and allow only the longer pigment-forming rays to pass. For example, ordinary dark-coloured cosmetic face powders and creams prevent or reduce the passage of moderate ultra-violet irradiation, but at the same time prevent *suntan*. Calamine lotion also has a screening value by forming a physical barrier, as has a lotion such as:—

Zinc oxide	60 minims (3.6 c.cm.)
Glycerin	1 ounce (28.4 c.cm.)
Rose water	to 3 ounces (85 c.cm.)

A more effective protective in the "sunshade" category is:—

(A) Light kaolin	300 minims (18 c.cm.)
Calamine lotion	to 10 ounces (283 c.cm.)
(B) Strong solution of ferric chloride	30 minims (1.8 c.cm.)
Water	to 5 ounces (142 c.cm.)

Pour B into A, stirring hard. Stand for twenty-four hours and add 30 minims (1.8 c.cm.) of arachis oil.

cludes aspirin, phenacetin, amidopyrine, and phenazone, are quite different. None of these drugs will relieve really severe pain, and they are mainly of value in headache, toothache, menstrual pain and "chronic rheumatism". All are antipyretics and may cause difficulty in interpreting the temperature chart. Aspirin, although comparatively safe, can cause hæmatemesis; phenacetin may give rise to methæmoglobinuria; amidopyrine has on several occasions produced agranulocytosis, and phenazone has a liability to cause drug rashes. This series of drugs has no sedative effect and must be combined with a barbiturate when sleep is required.

METHODS OF ASSESSING ANALGESIC ACTIVITY

The search for new analgesic drugs has stimulated investigation into methods for assessing analgesic activity. Three main techniques have been developed. Observations may be made on animals, or on man, either in the laboratory or in the wards. The most widely used experimental method, both in animals and in man, is based upon a technique first described by Wolff, Hardy and Goodell (1940).

The beam from an electric lamp is concentrated for three seconds on a blackened area of a subject's forehead, and the radiant energy is raised until the sensation of heat is changed to one of pain. This method, like most subjective methods, is difficult to control, and although it has yielded interesting results in man in the hands of its originators, it has been less successful when used by others (Dodds, Lawson, Simpson and Williams, 1945; Thorp, 1946). On the other hand, if the rat's tail is used instead of the human forehead, it seems possible to obtain consistent results; the end-point is taken as the time when the animal removes its tail from the painful stimulus. Using this method it has been shown that diamorphine (heroin) is about seven times as potent as morphine (Thorp, 1946), and that codeine is about five times less potent (Davies, Raventos and Walpole, 1946). Another method which yields consistent results in animals is that of Woolfe and Macdonald (1944), in which the threshold of mice to thermal pain is estimated by their behaviour on a hot plate. Unfortunately in animals it is never possible to be certain whether pain is being relieved by analgesics, or a reflex prevented, since, if the cerebral cortex is removed, similar responses to peripheral stimuli still occur.

Controlled observations on patients suffering from painful diseases are difficult to carry out, but are especially valuable, since the results have an immediate clinical significance. Thus Hayman and Fox (1937) found that ward sisters and house officers could not distinguish between the effects of omnopon and morphine in equivalent dosage, when tablets identical in appearance were used. This method can, however, only be used satisfactorily when the drugs to be compared differ little from one another. I have found that patients rapidly learnt to recognize the difference between morphine and physeptone by the greater sedative effect of the former.

CURRENT THERAPEUTICS

VII.—THE NEWER ANALGESICS

By E. J. WAYNE, M.D., F.R.C.P.

Professor of Pharmacology and Therapeutics, University of Sheffield; Physician, Sheffield Royal Infirmary and Hospital, and Sheffield Children's Hospital.

PAIN is the most common symptom for which a patient seeks medical advice, and the problem of its relief has exercised the mind of man since he first became capable of rational thought. Until the middle of last century, remedies were given by mouth, and were crude extracts of plants such as laudanum, or alcoholic preparations such as brandy. Pure morphine was isolated from opium by Sertürner in 1816, and it is a remarkable fact that, in spite of intensive research for a satisfactory substitute, it remains to this day the most widely used analgesic drug. A new approach to the problem began with the synthesis of acetanilide in 1866, and of aspirin in 1899. During the present century, research has proceeded on two main lines. First, attempts have been made to modify the molecule of morphine, so that its desirable effects are reproduced without the retention of undesirable side-effects; of these, the most important is its liability to cause addiction. Secondly, entirely new compounds have been found which possess the property of relieving pain, and subsequent research has been directed towards modifying their molecular structure so as to increase their activity.

It is desirable, in the first place, to look at the well-established drugs which are available, so as to see in what way they fall short of the ideal analgesic. The outstanding property of the morphine series is their capacity to relieve really severe pain, and so far no synthetic substitute has proved quite so efficacious. In addition, this group tends to produce euphoria and drowsiness, largely by diminishing the interest of the patient in the external world. It is this relief from apprehension which allays the restlessness of patients suffering from hæmorrhage, and which renders the opium alkaloids so valuable in conditions such as congestive cardiac failure. To produce comparable effects, the purely analgesic drugs must be combined with a sedative such as chloral or a barbiturate. The chief drawbacks of the opium group are their tendency to produce addiction, their liability to cause constipation, and their depressant effect on the respiratory centre. In special cases, however, these effects may be unimportant, or may even be turned to good account. Thus in inoperable carcinoma, addiction is of no importance, and in the treatment of diarrhœa and unproductive cough, morphine and codeine are useful drugs. There is indeed a place in therapy for the yet undiscovered drug which will relieve chronic diarrhœa as effectively as morphine, without diminishing the patient's interest in life.

The defects of the so-called "aromatic group" of analgesics, which in-

cludes aspirin, phenacetin, amidopyrine, and phenazone, are quite different. None of these drugs will relieve really severe pain, and they are mainly of value in headache, toothache, menstrual pain and "chronic rheumatism". All are antipyretics and may cause difficulty in interpreting the temperature chart. Aspirin, although comparatively safe, can cause hæmatemesis; phenacetin may give rise to methæmoglobinuria; amidopyrine has on several occasions produced agranulocytosis, and phenazone has a liability to cause drug rashes. This series of drugs has no sedative effect and must be combined with a barbiturate when sleep is required.

METHODS OF ASSESSING ANALGESIC ACTIVITY

The search for new analgesic drugs has stimulated investigation into methods for assessing analgesic activity. Three main techniques have been developed. Observations may be made on animals, or on man, either in the laboratory or in the wards. The most widely used experimental method, both in animals and in man, is based upon a technique first described by Wolff, Hardy and Goodell (1940).

The beam from an electric lamp is concentrated for three seconds on a blackened area of a subject's forehead, and the radiant energy is raised until the sensation of heat is changed to one of pain. This method, like most subjective methods, is difficult to control, and although it has yielded interesting results in man in the hands of its originators, it has been less successful when used by others (Dodds, Lawson, Simpson and Williams, 1945; Thorp, 1946). On the other hand, if the rat's tail is used instead of the human forehead, it seems possible to obtain consistent results; the end-point is taken as the time when the animal removes its tail from the painful stimulus. Using this method it has been shown that diamorphine (heroin) is about seven times as potent as morphine (Thorp, 1946), and that codeine is about five times less potent (Davies, Raventos and Walpole, 1946). Another method which yields consistent results in animals is that of Woolfe and Macdonald (1944), in which the threshold of mice to thermal pain is estimated by their behaviour on a hot plate. Unfortunately in animals it is never possible to be certain whether pain is being relieved by analgesics, or a reflex prevented, since, if the cerebral cortex is removed, similar responses to peripheral stimuli still occur.

Controlled observations on patients suffering from painful diseases are difficult to carry out, but are especially valuable, since the results have an immediate clinical significance. Thus Hayman and Fox (1937) found that ward sisters and house officers could not distinguish between the effects of omnopon and morphine in equivalent dosage, when tablets identical in appearance were used. This method can, however, only be used satisfactorily when the drugs to be compared differ little from one another. I have found that patients rapidly learnt to recognize the difference between morphine and physeptone by the greater sedative effect of the former.

DERIVATIVES OF THE OPIUM ALKALOIDS

A vast amount of work has been carried out in an attempt to find a potent analgesic without the undesirable properties of morphine. More than 120 compounds related to morphine have been synthesized, but comparatively few have survived clinical trial. Of the drugs with an established reputation, *diamorphine* (heroin) has the advantage of producing less constipation and nausea than morphine, but it has a much greater liability to give rise to addiction. On this account, its importation and manufacture in the United States are prohibited by law. *Codeine* is much safer than morphine, and has far less tendency to cause addiction. It is, however, a relatively weak analgesic, and if used for this purpose must be given in full doses of 60 mgm. (1 grain). *Dihydromorphinone* (dilaudid) is about five times as strong an analgesic as morphine and the average adult dose is 2 to 4 mgm. ($1/32$ to $1/16$ grain). It has rather less hypnotic effect, and is less liable to cause vomiting and constipation, properties which make it occasionally a desirable alternative to morphine. Unfortunately it is a drug of addiction. It may be used in the short-term treatment of painful conditions such as myocardial infarction and abdominal emergencies, when the emetic action of morphine is especially undesirable.

Metopon (methyl dihydromorphinone).—This substance is twice as effective an analgesic as morphine, and its duration of action is about the same. It has hardly any emetic effect and gives little or no respiratory depression; it is much less liable to produce mental dullness than morphine. Tolerance develops very slowly and disappears more quickly than when morphine is used. It is effective when given by mouth, but is, however, liable to cause addiction. At present it is available only in the United States, and then only to physicians who are prepared to keep a record card for every patient to whom it is administered. It may only be used in patients with inoperable cancer who need prolonged relief from pain. Its great advantage over morphine is the absence of mental dullness and nausea, and the slow development of tolerance and dependence. The dose is 6 mgm. repeated only when pain recurs (*J. Amer. Med. Ass.*, 1947).

Synthetic analogues of morphine.—Morphine is a derivative of phenanthrene, and since diphenylethylamine has a somewhat similar structure, Dodds, Lawson and Williams (1944) prepared 17 derivatives and studied their analgesic activity. Diphenylethylamine itself, in doses of 200 mgm., relieved pain, but caused mental confusion. β -hydroxy- $\alpha\beta$ -diphenylethylamine relieved pain effectively, but only when there was nerve pressure, and it had no effect on pain caused by inflammatory processes.

SYNTHETIC ANALGESICS

Bromo-aspirin (acetyl-5-bromosalicylic acid).—This compound has been investigated by Kranz, Iwamoto and Farson (1946), who report favourably on the absence of toxic effects. It is said to be more potent and longer lasting

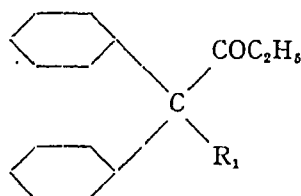
in its effects than aspirin, and to have double the analgesic effect of acetanilide. A dose of 0.6 gm. (9 grains) is recommended.

Pethidine (dolantin, demerol, isonipecaine, merperidine N.N.R.).—This substance was introduced by Eisleb and Schaumann in 1939. Chemically, it is a member of a group of piperidine compounds, resembling in structure atropine rather than morphine. Its effects on the pupils, heart and bronchi resemble those of atropine, but it also has a papaverine type of action on the gut and blood vessels. It possesses a slight local anæsthetic action. Like morphine, it has an analgesic action due to its effect on the central nervous system. The relief of pain is not so complete as with morphine, but is greater than that produced by codeine or aspirin. Drowsiness occurs after full doses. The cough, respiratory and vomiting centres are little affected. Pethidine in man has no effect on the electrocardiogram or basal metabolic rate. It can be shown to reduce localized spasm in the intestine, without influencing its propulsive power (Batterman, 1943). In general, visceral pain responds more completely than pain arising from skeletal and nervous structures. The drug is rapidly destroyed by the liver, and little is excreted in the urine, which probably explains its rather short action and lack of cumulative effects (Lehman and Aitken, 1942-43). Numerous reports of clinical trials are available (Batterman, 1943; Batterman and Mulholland, 1943; Christie, 1943; North, Hecht and Yonkman, 1944). There is fairly general agreement that pethidine is a valuable substitute for morphine in the relief of pain, the intensity of its effect lying between that of morphine and the aromatic analgesics. Special attention has been directed to its place in *obstetric practice*. The available evidence, together with a report on five hundred cases personally observed, has been well summarized by Barnes (1947). A single injection of 100 mgm. was adequate for the majority of labours, and a high proportion of the remainder required only 200 mgm. Good analgesia was experienced by 55 per cent. of mothers, and some relief obtained by 87 per cent. Pethidine did not shorten the duration of labour as has been claimed by some authors. It produced no tendency to post-partum hæmorrhage, and foetal anoxia was rare. Barnes concludes that pethidine approaches the ideal obstetric analgesic more closely than any other drug in common use.

The *toxic effects* of pethidine are few, but occur fairly frequently with doses of 100 mgm. and over. The most common is dizziness, but sweating and nausea may occur. In prolonged overdosage, or in acute poisoning, atropine-like effects predominate, e.g., dilated pupils, dry mouth, tachycardia, cerebral irritability and convulsions. There is, however, a wide margin of safety. There is evidence that pethidine should not be used in patients with intracranial lesions in whom respiratory embarrassment readily occurs (Guttman, 1944). The single greatest drawback to the wider use of pethidine, however, is its tendency to produce *addiction*. For this reason, it has been placed under the Dangerous Drugs Act. Polonio (1947)

has reviewed the position, using as a basis his personal observation of 15 cases. Two deaths occurred. The daily dose ranged from 0.3 to 14.0 gm., i.e., up to 28 times the maximum safe daily dose. Addicts usually take the drug by injection. It gives rise to short sleep and intellectual dullness. Withdrawal symptoms are, however, mild, and with hospital treatment recovery is usually rapid. The *uses* of pethidine are limited by this tendency to produce addiction, but it is undoubtedly a valuable drug for occasional use in cases in which spasm of smooth muscle is giving rise to pain, e.g. biliary and intestinal colic. It may be used pre- or post-operatively, when the absence of the side-effects of morphine is an advantage. It is unquestionably worth consideration as an obstetric analgesic. In dysmenorrhœa and asthma caution should be observed. Although a *dose* of 25 mgm. will often give an effect and should be tried, the usual certainly effective dose is 100 mgm. by mouth or intramuscular injection. Not more than 400 mgm. should be given in twenty-four hours.

Physeptone (dolophine, amidone, methadon, miadone, adanon, diamion, AN 148).—This substance is one of several analgesic drugs prepared by German chemists and reinvestigated in Britain and the United States after the war. They have the general formula:—



In physeptone R_1 is $\text{CH}_2\cdot\text{CH}(\text{CH}_3)\cdot\text{N}(\text{CH}_3)_2$.

Observation on animals show that it is an effective analgesic. In man, using Wolff, Hardy and Goodell's method (1940), 5 mgm. was found to cause definite analgesia (Scott and Chen, 1946). Hewer and Keele (1947) compared the effect of physeptone, pethidine and morphine on the pain of muscular ischæmia in human volunteers. It was found that 7.5 mgm. was equivalent to 7.5 mgm. morphine or 75 mgm. pethidine. It produced as much euphoria, but less giddiness and blurring of vision than pethidine. Physeptone in full doses depresses the respiratory centre, but to a less extent than morphine, and it does not affect the heart or blood pressure. It increases the tone of the intestine, due to a central action (Scott, Livingstone, Jacoby and Broberg, 1947). Tolerance was not produced in dogs during 28 days continuous administration (Scott and Chen, 1946). Up to 35 per cent. is excreted in the urine in man; the fate of the remainder is unknown. Favourable reports on the clinical use of physeptone have been published (Scott, C. C., and co-workers, 1947; Scott, W. W., and co-workers, 1947; Troxil, 1948). The first group of workers found that the

drug failed to give some relief in only 8 of 210 patients. Troxil (1948) states that 10 mgm. is as effective as 15 mgm. of morphine or 150 mgm. pethidine, and effective relief of pain was achieved in 81 per cent. of 400 patients. Oral administration is almost as effective as hypodermic injection. Physeptone differs from morphine chiefly in the lesser degree of sedation and narcosis which it produces, and in a lesser tendency to produce nausea and vomiting. It has a depressant action on the cough centre, and has been used in pulmonary tuberculosis for this purpose (Scott, C. C., and co-workers, 1947). Prescott and Ransom (1947) have compared physeptone and pethidine as obstetric analgesics. Both were effective and little difference was observed, except in the greater liability of physeptone to produce depression of respiration in the baby. The effect was, however, sufficiently marked to render physeptone an undesirable drug for the relief of pains of childbirth. *The toxic effects* of physeptone are, in order of frequency, light-headedness or dizziness, nausea, dryness of the mouth, diaphoresis, and mental depression. They occurred in 13 per cent. of 400 patients treated by Troxil (1948). *Addiction* appears to be less likely than with pethidine since physeptone produces less euphoria (Prescott and Ransom, 1947). In the monkey, neither physical dependence nor tolerance occurred (Woods, Wyngaarden and SeEVERS, 1947). Troxil (1948) observed slight tolerance but no evidence of addiction in patients during two to three months' treatment. Abstinence symptoms from morphine can be controlled by physeptone, and when the latter drug is then abruptly withdrawn, symptoms are much milder than when morphine is discontinued without preliminary physeptone administration (Isbell, Wikler, Eisenman and Frank, 1947). In spite of these observations, however, it has been thought desirable to place physeptone under the Dangerous Drugs Act.

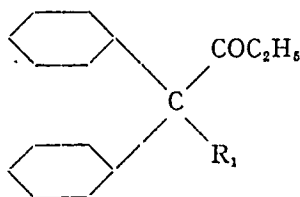
The uses of this drug are mainly in conditions in which the relief of pain is desirable without narcosis, and without the nausea which morphine so often causes. By combining it with a short-acting barbiturate (e.g. hexobarbitone) or with hyoscine, a controllable degree of sedation can be produced, and it can be used pre- or post-operatively. In pain due to spasm of smooth muscle it is less effective than pethidine, but is probably of more value in pain arising from nerves, bones or joints. In inoperable carcinoma the failure to produce tolerance is an advantage. The *dose* of physeptone, which is certainly effective in the majority of patients, is 10 mgm., but initial doses of 2.5 or 5.0 mgm. should always be tried. The drug is effective orally but can be given intramuscularly or intravenously. As much as 30 mgm. four-hourly has been given without ill-effects, but such high dosage is undesirable except in very severe pain.

CONCLUSION

Those who wish to explore for themselves the value of the newer analgesics, are advised to try pethidine in cases in which pain accompanies smooth

has reviewed the position, using as a basis his personal observation of 15 cases. Two deaths occurred. The daily dose ranged from 0.3 to 14.0 gm., i.e., up to 28 times the maximum safe daily dose. Addicts usually take the drug by injection. It gives rise to short sleep and intellectual dullness. Withdrawal symptoms are, however, mild, and with hospital treatment recovery is usually rapid. The *uses* of pethidine are limited by this tendency to produce addiction, but it is undoubtedly a valuable drug for occasional use in cases in which spasm of smooth muscle is giving rise to pain, e.g. biliary and intestinal colic. It may be used pre- or post-operatively, when the absence of the side-effects of morphine is an advantage. It is unquestionably worth consideration as an obstetric analgesic. In dysmenorrhœa and asthma caution should be observed. Although a *dose* of 25 mgm. will often give an effect and should be tried, the usual certainly effective dose is 100 mgm. by mouth or intramuscular injection. Not more than 400 mgm. should be given in twenty-four hours.

Physeptone (dolophine, amidone, methadon, miadone, adanon, diamidon, AN 148).—This substance is one of several analgesic drugs prepared by German chemists and reinvestigated in Britain and the United States after the war. They have the general formula:—



In *physeptone* R₁ is CH₂.CH(CH₃). N(CH₃)₂.

Observation on animals show that it is an effective analgesic. In man, using Wolff, Hardy and Goodell's method (1940), 5 mgm. was found to cause definite analgesia (Scott and Chen, 1946). Hewer and Keele (1947) compared the effect of *physeptone*, pethidine and morphine on the pain of muscular ischæmia in human volunteers. It was found that 7.5 mgm. was equivalent to 7.5 mgm. morphine or 75 mgm. pethidine. It produced as much euphoria, but less giddiness and blurring of vision than pethidine. *Physeptone* in full doses depresses the respiratory centre, but to a less extent than morphine, and it does not affect the heart or blood pressure. It increases the tone of the intestine, due to a central action (Scott, Livingstone, Jacoby and Broberg, 1947). Tolerance was not produced in dogs during 28 days continuous administration (Scott and Chen, 1946). Up to 35 per cent. is excreted in the urine in man; the fate of the remainder is unknown. Favourable reports on the clinical use of *physeptone* have been published (Scott, C. C., and co-workers, 1947; Scott, W. W., and co-workers, 1947; Troxil, 1948). The first group of workers found that the

REVISION CORNER

HYPERTRICHOSIS (Hirsuties)

HYPERTRICHOSIS (hirsuties) may be defined as an excessive development of hair which may be localized, or may affect numerous areas of the body. The localized abnormal formation of hair may be found over the lower region of the back in connexion with spina bifida, or it may only be excessive in parts normally hairy, such as the forearms and legs. Its abnormality is commonly due to its appearance, usually with a male distribution, in the female sex. Excessive growth of hair may be found over some moles, and extensive growth of long down-like hairs may occur in the skin of the large dark pigmented patches which may be found in multiple neurofibromatosis (von Recklinghausen's disease).

CLINICAL DIAGNOSIS

Hirsutism in the female falls generally into three main groups. First, in young women who are otherwise perfectly healthy and normal; secondly, it may develop at the menopause, and lastly, it may be found in cases associated with gross genital abnormalities. This last group, although of much interest and importance from the point of view of investigation, diagnosis and treatment, is fortunately rare and only amounts to a few per cent. of the total cases. In the last group the causes of the hirsutism may be hyperplasia or tumour formation in the cortex of the suprarenal (adreno-genital syndrome); a virilizing ovarian tumour or arrhenoblastoma (ἄρρην = masculine); a basophil adenoma of the anterior lobe of the pituitary (Cushing's syndrome); very rarely a pineal tumour; internal hydrocephalus possibly affecting the pituitary, caused, for example, by an ependymitis of the aquæduct of Sylvius, and lastly, in some cases of bronzed diabetes (Achar'd type). To exclude these different conditions such patients will require a complete clinical examination. A gynæcological examination should be made to see whether an arrhenoblastoma is present or not. X-ray examination of the skull may be necessary to observe the appearance of the pituitary fossa. In children with precocious growth, X-ray of the bones, particularly of the hands and wrists, may be done to determine the bone age of the individual. Intravenous pyelograms may be performed to see whether or not an adrenal tumour may be causing distortion of the renal pelvis and calices. If an adrenal tumour is suspected, X-ray examination after peri-renal insufflation of air may be performed, but may usually be dispensed with as it is not free from risk.

The *urinary excretion of hormones* should be investigated. A twenty-four hour specimen of urine should have the 17-keto-steroid content estimated, and it may be of interest to estimate the pregnanediol excretion as well. The normal excretion of 17-keto-steroid in a healthy woman is about 3.5 to 15 mgm. daily. In cases of virilism due to the adreno-genital syndrome, it may be over 100 mgm. daily. In women with hirsutism who are otherwise normal the excretion of 17-keto-steroids may be somewhat increased. In a series of such cases, not yet published, examined by Dr. Bradshaw at the Rotunda Hospital, Dublin (personal communication), it was found that the 17-keto-steroid excretion was approximately double the normal value.

In some cases of the adreno-genital syndrome associated with *pseudo-hermaphroditism* it may be necessary to perform a laparotomy to determine the true sex of the individual and to palpate the suprarenals. If there is a tumour of the cortex of the suprarenal, or if there is hyperplasia of one or both suprarenals, the tumour or larger suprarenal should be removed, but this should not be done before it has been determined that there is a suprarenal gland present on the other side. Fatalities have occurred from the neglect of this precaution. A psychological study of the patients should be made to see whether they have normal sex instincts or

muscle spasm, and as an obstetric analgesic. Physeptone given by mouth, and if necessary given in conjunction with a barbiturate, may save the practitioner an evening journey to inject morphine, and such treatment can be continued for some time with only slight danger of producing addiction, and with no tendency to constipation.

In conclusion, it may be safely prophesied that the drugs at present available for the relief of pain will eventually be replaced by compounds with still fewer side-effects. The ingenuity of the organic chemist may yet devise a very close approximation to the "ideal analgesic" of the pharmacologist.

References

- Barnes, J. (1947): *Brit. med. J.*, **i**, 437.
 Batterman, R. C. (1943): *Arch. intern. Med.*, **71**, 345.
 —, and Mulholland, J. H. (1943): *Arch. Surg.*, **46**, 404.
 Christie, R. V. (1943): *Lancet*, **i**, 294.
 Dodds, E. C., Lawson, W., and Williams, P. C. (1944): *Proc. Roy. Soc., B.* **132**, 119.
 —, —, Simpson, S. A., and Williams, P. C. (1945): *J. Physiol.*, **104**, 47.
 Davies, O. L., Raventos, J., and Walpole, A. L. (1946): *Brit. J. Pharmacol.*, **i**, 255.
 Eisleb, O., and Schaumann, O. (1939): *Dtsch. med. Wschr.*, **65**, 967.
 Guttman, S. A. (1944): *J. Amer. med. Ass.*, **124**, 155.
 Hayman, J. M., and Fox, H. (1937): *Ibid.*, **109**, 1813.
 Hewer, A. J. H., and Keele, C. A. (1947): *Lancet*, **ii**, 281.
 Isbell, H., Wikler, A., Eisenman, A. J., and Frank, K. (1947): *Federation Proc.*, **6**, 341.
Journal of the American Medical Association (1947): Editorial, **134**, 291.
 Krantz, J. C., Iwamoto, H. K., and Farson, de C. B. (1946): *Curr. Res. Anesth.*, **25**, 221.
 Lehman, R. A., and Aitken, T. (1942-43): *J. Lab. clin. Med.*, **28**, 787.
 North, P. S., Hecht, H., and Yonkman, F. F. (1944): *Ann. intern. Med.*, **21**, 17.
 Polonio, P. (1947): *Lancet*, **i**, 592.
 Prescott, F., and Ransom, S. G. (1947): *Ibid.*, **ii**, 501.
 Scott, C. C., and Chen, K. K. (1946): *J. Pharmacol.*, **87**, 63.
 —, Kohlstaedt, K. G., and Chen, K. K. (1947): *Curr. Res. Anesth.*, **26**, 12.
 Scott, W. W., Livingstone, H. M., Jacoby, J. J., and Broberg, G. R. (1947): *Ibid.*, **26**, 18.
 Thorp, R. H. (1946): *Brit. J. Pharmacol.*, **1**, 113.
 Troxil, E. B. (1948): *J. Amer. med. Ass.*, **136**, 920.
 Wolff, H. G., Hardy, J. D., and Goodell, H. (1940): *J. clin. Invest.*, **19**, 659.
 Woods, L. A., Wyngaarden, J. B., and Seevers, M. H. (1947): *Proc. Soc. exp. Biol.*, **65**, 113.
 Woolfe, G., and Macdonald, A. D. (1944): *J. Pharmacol.*, **80**, 300.

the hair follicle to the bulb and a current of 1 or 2 milliamperes is allowed to flow for 4 or 5 seconds. The lower end of the follicle is coagulated in this way and the hair can be withdrawn. The epilated area should be treated with weak zinc ionization immediately afterwards to prevent pock markings.

In the menopausal cases stilbæstrol should be prescribed to relieve the other menopausal symptoms, although it will have no action on the hypertrichosis.

GERALD DOCKERAY, M.D., M.Sc., F.R.C.P.I.

THE CLICKING JAW

CLICKING of the temporo-mandibular joint is by no means an uncommon complaint. It is invariably due to derangement of the fibro-cartilage disc, which may either be loose or enlarged, so that it is buckled during the advance of the condyle of the mandible in opening the mouth. Alternatively, the mouth may open naturally and the disc may be so displaced as to block the return of the condyle to the articular fossa; in which event the joint remains locked open. Most patients relate their early symptoms to a traumatic incident. Such trauma may be self-inflicted, as for instance, by a particularly wide yawn, or it may be the result of a blow from boxing or a fall on the chin. Many cases can be traced to dental extractions, usually of molar teeth, and usually when nitrous oxide has been the anæsthetic agent. As the result of the initial displacement, the disc remains loose, and repeated twisting and snapping causes it to become enlarged and aggravates the symptoms. Other patients develop the derangement as the result of degenerative changes in the disc which are brought about by prolonged strain of the joint consequent upon malocclusion. If the molar surfaces meet on one side a little ahead of the other side, there is an excessive strain, both on the temporo-mandibular joint and on the alveolar bone, with the result that the teeth, over a period of years, become displaced, and arthritic changes occur in the joint. Sometimes the condition follows fairly quickly after the removal of a solitary molar on one side of the upper or lower jaw. Primary arthritis of the jaw is rare and is most often due to gonococcal infection.

TREATMENT

In the management of these patients a readjustment of the dental surfaces is essential, and defective molar height must be made good by dentures; if there is malocclusion in the presence of adequate masticating surfaces, then the molars which meet first must be ground down until the jaws oppose symmetrically. If there is a recent history of trauma, a period of complete splintage by interdental wiring may allow the condition to resolve without becoming chronic. Unfortunately most cases have developed distortion of the disc by the time they present for treatment. In diagnosis, when the jaw is opened, the midline may deviate towards the affected side if the condyle is held up by the forwardly displaced disc; deviation may occur away from the affected side if the condyle descends over a thick disc, or, during closing, the disc prevents the return of the condyle. Radiography may reveal the presence of bone changes but it does not help particularly in deciding upon treatment. When the dental balance has been appropriately corrected, if there is no improvement in the symptoms after a month, exploration of the joint will be required. From the patient's point of view the disabilities may be:—

- (1) Inability to open the mouth wide enough to take a normal bite of food.
- (2) Snapping of the jaw during ordinary movement.
- (3) Locking of the jaw, closed or open.
- (4) Continual pain in the jaw referred to almost any area of the trigeminal supply.

If the patient complains of pain and stiffness in the morning with an improvement after the first meal, physiotherapy in the form of short-wave diathermy may produce marked benefit by relieving the arthritis. No amount of physiotherapy or dental treatment will, however, correct a joint in which the disc is either too big or too loose.

whether there is homosexuality present. There will often be other psychological disturbances due to their unfortunate condition. Some pseudo-hermaphrodites may be stronger and more athletic than normal girls; one patient seen by me was outstandingly successful as a hockey player. In addition to hirsutism, the patient may have a beard or need to shave frequently; the hair of the head may fall out and the woman may be quite bald on the vertex and in the temporal region. When a tumour or suprarenal gland is to be removed the patient should be given 10 c.cm. of cortical extract daily for ten days preceding operation and for a month afterwards. It may be necessary to give larger doses in the postoperative period. The operation specimen should be weighed. A normal suprarenal weighs about 5 gm., and a hyperplastic gland may weigh about 20 gm. In the subsequent histological examination sections should be stained with Ponceau-fuchsin (Vine's stain), as in cases of the adreno-genital syndrome the cortical cells contain numerous reddish-brown granules when stained in this way. If the cause of the virilism is an arrhenoblastoma the tumour should be stained for fat. If the tumour of the ovary is benign the abnormal hair falls out within a few days of the operation. If it is malignant the signs of virilism will recur simultaneously with the formation of metastases.

The signs of virilism are (1) hirsuties; (2) enlargement of the clitoris; (3) deepening of the voice. A large clitoris should be removed but the deepening of the voice is permanent owing to the alterations in the larynx being irreversible. Such signs as shrinkage of the breasts and amenorrhœa are not primary signs of virilism but are only of a secondary nature.

In cases of pseudo-hermaphroditism with absence of the vagina, an artificial vagina may be formed by the Read and McIndoe technique, using a skin graft from the thigh, shaped round a perspex mould the size and shape of a vagina. The mould is placed in position by careful blunt dissection between the urethra and rectum. Patients have in some cases subsequently had the cervix brought into the top of the artificial vagina and have become pregnant, requiring of course to be delivered by Cæsarean section.

In the *Cushing syndrome* (pituitary basophilism) hypertrichosis is present as in the adreno-cortical syndromes, with changes in the skin which may give the patient a plethoric appearance. Purplish *linæ atrophicæ* may be present on the obese abdomen. Hypertension is present with erythræmia, ecchymoses and glycosuria. The 17-keto-steroid estimation will help in the diagnosis as this is not increased as in the adreno-genital syndrome. An enlarged clitoris also makes the adreno-genital syndrome more likely.

TREATMENT

These somewhat rare conditions having been ruled out and the patient having been found to be otherwise healthy it will be necessary to advise treatment. They should if young be told that it is quite usual for a person with hypertrichosis to be able to have an infant and feed it from the breast. They should be advised to use a razor. This suggestion will usually be found unwelcome and the objections will be advanced that shaving makes the hair more coarse and that it makes it grow more rapidly. To meet the first objection they may be told that if the bristles of a soft brush were cut across near their bases the hair of the brush would feel hard and coarse although they were otherwise unaltered, and the second objection should be met by saying that in most cases the condition tends to be progressive so that the hair will probably grow faster in any event. Other forms of treatment may be discussed with the patient for the purpose of condemning them. X-rays should not be considered as they cause atrophy of the skin, telangiectases and sometimes pruritus. Depilatory powders and creams made up of such substances as barium sulphide burn the hairs at the skin level. They redden the skin and stimulate growth. Epilation with tweezers may cause chronic folliculitis. Electrolysis is expensive, slow and painful, but may be used when there are only a limited number of hairs to be eradicated.

In electrolysis a fine rounded platinum needle attached to a negative pole is passed into

the hair follicle to the bulb and a current of 1 or 2 milliamperes is allowed to flow for 4 or 5 seconds. The lower end of the follicle is coagulated in this way and the hair can be withdrawn. The epilated area should be treated with weak zinc ionization immediately afterwards to prevent pock markings.

In the menopausal cases stilbæstrol should be prescribed to relieve the other menopausal symptoms, although it will have no action on the hypertrichosis.

GERALD DOCKERAY, M.D., M.Sc., F.R.C.P.I.

THE CLICKING JAW

CLICKING of the temporo-mandibular joint is by no means an uncommon complaint. It is invariably due to derangement of the fibro-cartilage disc, which may either be loose or enlarged, so that it is buckled during the advance of the condyle of the mandible in opening the mouth. Alternatively, the mouth may open naturally and the disc may be so displaced as to block the return of the condyle to the articular fossa; in which event the joint remains locked open. Most patients relate their early symptoms to a traumatic incident. Such trauma may be self-inflicted, as for instance, by a particularly wide yawn, or it may be the result of a blow from boxing or a fall on the chin. Many cases can be traced to dental extractions, usually of molar teeth, and usually when nitrous oxide has been the anæsthetic agent. As the result of the initial displacement, the disc remains loose, and repeated twisting and snapping causes it to become enlarged and aggravates the symptoms. Other patients develop the derangement as the result of degenerative changes in the disc which are brought about by prolonged strain of the joint consequent upon malocclusion. If the molar surfaces meet on one side a little ahead of the other side, there is an excessive strain, both on the temporo-mandibular joint and on the alveolar bone, with the result that the teeth, over a period of years, become displaced, and arthritic changes occur in the joint. Sometimes the condition follows fairly quickly after the removal of a solitary molar on one side of the upper or lower jaw. Primary arthritis of the jaw is rare and is most often due to gonococcal infection.

TREATMENT

In the management of these patients a readjustment of the dental surfaces is essential, and defective molar height must be made good by dentures; if there is malocclusion in the presence of adequate masticating surfaces, then the molars which meet first must be ground down until the jaws oppose symmetrically. If there is a recent history of trauma, a period of complete splintage by interdental wiring may allow the condition to resolve without becoming chronic. Unfortunately most cases have developed distortion of the disc by the time they present for treatment. In diagnosis, when the jaw is opened, the midline may deviate towards the affected side if the condyle is held up by the forwardly displaced disc; deviation may occur away from the affected side if the condyle descends over a thick disc, or, during closing, the disc prevents the return of the condyle. Radiography may reveal the presence of bone changes but it does not help particularly in deciding upon treatment. When the dental balance has been appropriately corrected, if there is no improvement in the symptoms after a month, exploration of the joint will be required. From the patient's point of view the disabilities may be:—

- (1) Inability to open the mouth wide enough to take a normal bite of food.
- (2) Snapping of the jaw during ordinary movement.
- (3) Locking of the jaw, closed or open.
- (4) Continual pain in the jaw referred to almost any area of the trigeminal supply.

If the patient complains of pain and stiffness in the morning with an improvement after the first meal, physiotherapy in the form of short-wave diathermy may produce marked benefit by relieving the arthritis. No amount of physiotherapy or dental treatment will, however, correct a joint in which the disc is either too big or too loose.

whether there is homosexuality present. There will often be other psychological disturbances due to their unfortunate condition. Some pseudo-hermaphrodites may be stronger and more athletic than normal girls; one patient seen by me was outstandingly successful as a hockey player. In addition to hirsutism, the patient may have a beard or need to shave frequently; the hair of the head may fall out and the woman may be quite bald on the vertex and in the temporal region. When a tumour or suprarenal gland is to be removed the patient should be given 10 c.cm. of cortical extract daily for ten days preceding operation and for a month afterwards. It may be necessary to give larger doses in the postoperative period. The operation specimen should be weighed. A normal suprarenal weighs about 5 gm., and a hyperplastic gland may weigh about 20 gm. In the subsequent histological examination sections should be stained with Ponceau-fuchsin (Vine's stain), as in cases of the adreno-genital syndrome the cortical cells contain numerous reddish-brown granules when stained in this way. If the cause of the virilism is an arrhenoblastoma the tumour should be stained for fat. If the tumour of the ovary is benign the abnormal hair falls out within a few days of the operation. If it is malignant the signs of virilism will recur simultaneously with the formation of metastases.

The signs of virilism are (1) hirsuties; (2) enlargement of the clitoris; (3) deepening of the voice. A large clitoris should be removed but the deepening of the voice is permanent owing to the alterations in the larynx being irreversible. Such signs as shrinkage of the breasts and amenorrhœa are not primary signs of virilism but are only of a secondary nature.

In cases of pseudo-hermaphroditism with absence of the vagina, an artificial vagina may be formed by the Read and McIndoe technique, using a skin graft from the thigh, shaped round a perspex mould the size and shape of a vagina. The mould is placed in position by careful blunt dissection between the urethra and rectum. Patients have in some cases subsequently had the cervix brought into the top of the artificial vagina and have become pregnant, requiring of course to be delivered by Cæsarean section.

In the *Cushing syndrome* (pituitary basophilism) hypertrichosis is present as in the adreno-cortical syndromes, with changes in the skin which may give the patient a plethoric appearance. Purplish lineæ atrophicæ may be present on the obese abdomen. Hypertension is present with erythræmia, ecchymoses and glycosuria. The 17-keto-steroid estimation will help in the diagnosis as this is not increased as in the adreno-genital syndrome. An enlarged clitoris also makes the adreno-genital syndrome more likely.

TREATMENT

These somewhat rare conditions having been ruled out and the patient having been found to be otherwise healthy it will be necessary to advise treatment. They should if young be told that it is quite usual for a person with hypertrichosis to be able to have an infant and feed it from the breast. They should be advised to use a razor. This suggestion will usually be found unwelcome and the objections will be advanced that shaving makes the hair more coarse and that it makes it grow more rapidly. To meet the first objection they may be told that if the bristles of a soft brush were cut across near their bases the hair of the brush would feel hard and coarse although they were otherwise unaltered, and the second objection should be met by saying that in most cases the condition tends to be progressive so that the hair will probably grow faster in any event. Other forms of treatment may be discussed with the patient for the purpose of condemning them. X-rays should not be considered as they cause atrophy of the skin, telangiectases and sometimes pruritus. Depilatory powders and creams made up of such substances as barium sulphide burn the hairs at the skin level. They redden the skin and stimulate growth. Epilation with tweezers may cause chronic folliculitis. Electrolysis is expensive, slow and painful, but may be used when there are only a limited number of hairs to be eradicated.

In electrolysis a fine rounded platinum needle attached to a negative pole is passed into

X-ray of the lungs is needed. Staphylococcal infection of the skin, in the form of small angry-looking boils, is common. Otitis media and pyelitis are the other forms of infection most often diagnosed; but something more than a pink drum which retains the light reflex, or one or two pus cells per field by $\frac{1}{6}$ lens magnification, with a weak growth of coliform bacilli on culture, is needed for a diagnosis, either of otitis media or pyelitis. Such slight signs as the above are common intercurrent findings in any debilitated child. They do not merit vigorous saturation with penicillin or sulphonamides, the excretion of which in itself is an added load on an already incapacitated renal excretory mechanism. Be sure that infection exists before treating it. It is often impossible to be sure whether an infection is primary or secondary, as the impoverished resistance of the marasmic infant makes him an easy prey. Thrush is one of the most common secondary invaders.

CLINICAL SIGNS

The appearance of the severely marasmic infant is characteristic. The skull looks large in proportion to the wizened, senile-looking face with big staring eyes. Sucking pads on the cheeks are prominent, but subcutaneous fat is absent and the skin of the body is in folds; the abdomen is usually retracted. The extremities are red or bluish and cold, and often the temperature and pulse rate are subnormal. There is a tendency to the return of feeds, which in severe cases, plus infection, readily passes on to severe gastro-enteritis.

TREATMENT

For the mild case of marasmus, or simple atrophy, treatment at home is advisable, provided the mother's maternal instincts and the home conditions are favourable. In any severe case skilled nursing in a hospital, in a cubicle, is essential. Anyone attending or visiting the infant must wear a mask, and be scrupulously clean in the care of their hands. These infants stand cold badly and often have subnormal temperatures and bluish extremities. It is well to wrap the limbs in wool and cover with woollens, and also to provide a woollen bonnet. The temperature of the room should be kept at 65°F . (18.3°C). If wasting is severe, bathing with soap and water is inadvisable; rather treat as a premature, cleansing the skin and swabbing with olive oil.

The aim in *feeding* is to provide enough calories to meet the needs of the expected weight for age. This would mean giving many more than 50 calories for the body weight, which cannot be done abruptly, but must be introduced gradually. The number of feeds may need to be increased to seven, thereby giving the total daily quantity in smaller portions. Giving water by spoon between feeds is important in the maintenance of hydration. For the infant under three months, obtain breast milk if possible, or a half-cream acidified milk (Lacidac) in which the protein curd is flocculent. Over the age of three months infants do best to begin with on a humanized milk, Trufood, or Ostermilk No. 1. Additional carbohydrate is best added in the form of dextri-maltose, as it is easily assimilated and there is less fermentation than with cane sugar.

To improve *hydration* when turgor and elasticity of the skin are poor, an intravenous drip of Hartmann's solution is useful, following which, or separately, a transfusion of 70 to 80 c.cm. of whole blood or plasma helps to restore the plasma proteins, which tend to fall in states of chronic debility. As the kidney of the small infant is a relatively inefficient secretory organ in comparison to its functional powers in later life, drugs or antibiotics should not be given to the marasmic infant unless a definite need exists.

When the facilities of a laboratory are available and the blood chemistry can be investigated, many pitfalls await the unwary. A high blood urea (normal 15 to 40 mgm. per 100 c.cm.) will occur as a result of loss of body fluids reducing excretory activity, or because of a fall in blood pressure, or from an increase of nitrogen

Operative treatment is carried out through a vertical pre-auricular incision, or the pinna may be turned forwards and the jaw approached by cutting through both the anterior and posterior walls of the cartilaginous meatus. This latter approach gives a better exposure of the joint and, owing to the width of the condyle, it is often found that the deep attachment of the disc is at least an inch from the pre-auricular skin surface. The disc should be excised and great care must be taken to avoid slicing the articular surface of the condyle. If advanced roughening of the articular surfaces is present, insertion of a tantalum foil sheet may diminish the symptoms. After-treatment consists of bandage immobilization of the jaw and the taking of fluids only, for five days, after which jaw movement must be practised. The condyle tends to be held back after operation so that the lower jaw deviates to the affected side and the patient must train himself by pressing the mandible away from the affected side during jaw movements. Further adjustment of the articulation of the teeth may be necessary.

Although some patients worry unduly about a clicking jaw and develop what amounts to a "habit click", many of them who are treated by excision of the disc are so relieved as to be counted among the surgeon's most grateful patients. Broadly speaking the condition is comparable to lesions of the knee meniscus in that the damaged cartilage must be removed, although the prognosis depends upon the state of the joint surface, the component ligaments and synovial membrane. Prognosis is worse in those cases in which arthritis is established, but even then, as in the knee, the torn disc must be removed. Prevention of arthritis by early disc excision in selected cases should be the aim of treatment.

D. F. ELLISON NASH, F.R.C.S.

THE CARE OF THE MARASMIC INFANT

MARASMUS has lost much of its baleful significance. Its former pseudonyms for gradations in the state of undernutrition of the infant are seldom heard: infantile atrophy, dystrophy, athrepsia, and decomposition. This bogey has been dispelled largely by the dissemination of a better knowledge of infant feeding. Ignorance and poverty were its chief promoters.

CAUSAL FACTORS

One cause of chronic undernutrition, or marasmus, is to be sought in one of three factors: infection, faulty feeding, or the fault may be, though rarely is, in the infant itself. Fortunately, marasmus in the breast-fed infant is a rarity. In such an infant, at about two or three months of age, on an adequate intake and proper times of feeding, a level line on the weight chart, or a steady loss, persists for several weeks before a gradual improvement in nutrition is regained. All that can be postulated in the absence of infection is a defect of assimilation. The impulse to take the infant off the breast is almost irresistible, but the reasons for and against weaning must be carefully weighed.

More often it is the bottle-fed infant, improperly fed in quantity or quality, who fails to gain and loses weight. In all cases a check-up on calories is useful. An infant requires 50 calories per pound expected body weight for age per day; an ounce (28.4 c.cm.) of milk equals 20 calories, half-cream milk about 17 calories, a level teaspoonful of sugar, or 4 gm., 14 calories. Fat may be badly tolerated, the stools being rancid, often white or greenish with pellets of fat, curd, and some mucus. Excess carbohydrate leads to a distended belly, frequent acid loose stools, and red buttocks. When excess of protein, or cow's milk casein, is undigested, the stools may be grey and constipated. Increasing the quantity of feeds aggravates the constipation, and the weight still continues to fall.

Infection is probably the most common cause of marasmus. It is usually parenteral, mild and unattended by pyrexia. It may be a low-grade pneumonic infection, so an

of the resulting mixture lies between 7 and 9, that is, on the alkaline side of neutrality. In the case of magnesium oxide it will rise as high as 10, whilst bismuth carbonate will produce a pH of about 4, which is well on the acid side. Thus when administering alkalis the idea is to give sufficient to maintain the gastric contents more or less neutral in reaction, but in practice all that can be done is to ensure that the gastric contents are not highly acid. This may best be done by using a neutralizing agent such as magnesium trisilicate which, being practically insoluble in alkaline solutions, will not tend to produce alkalosis, even when present in excess, as some other antacids do. If magnesium trisilicate is actually present in excess over the acid secreted by the stomach, the pH of the stomach contents will be just on the alkaline side of neutrality. The inquirer makes an error in speaking of a "minimum pH" when he means, I believe, absolute neutrality or a pH of 7. A "minimum pH" would represent a highly acid solution.

(2) There is no short cut to carrying out estimations of the alkali reserve. It is true that the urine in a case of alkalosis which results from the excessive ingestion of alkali is always alkaline. If the freshly passed urine from a patient taking alkalis is acid to phenol red (i.e., it is of a pH of less than 6) the patient cannot be suffering from alkalosis of such cause, but no further conclusion could be drawn.

W. N. MANN, M.D., F.R.C.P.

Habitual Abortion

QUERY.—What should be the management of pregnancy in a woman of thirty-eight, who has had abortions at two and three months? Since the one six years ago she has had a dilatation and curetting. Have progestin and vitamin E any place in an effort to carry her over the danger period at the times of the missed menses?

REPLY.—Already six years have elapsed since the last pregnancy and the case warrants a full investigation for the delay in conception. Both husband and wife need to be fully examined. Tubal patency should be tested. The examination should include renal function tests. Vitamin E has no place in treatment. As for progesterone, here one is on more controversial ground. Abortion can occur even when progesterone is present in adequate amounts, as shown by estimation of pregnanediol in the urine. If the excretion of this substance is low the implantation of progesterone will probably not do any harm. On the other hand, if it is high such treatment may induce an abortion. The subject of habitual abortion is still very confused. The simplest, cheapest, and sometimes most effective

tive treatment is absolute rest in bed during the early months. Barbiturates should be given, but not morphine.

W. C. W. NIXON, M.D., F.R.C.S., F.R.C.O.G.

The "Safe Period" and Birth Control

QUERY.—In the issue of *The Practitioner* for March 1948, under the query "Temperature Charting in Relation to the Safe Period", there is no mention as to the safety of the period "after menstruation to the next ovulation". I shall be grateful if you could let me know what is the safe period. For those who do not like to use any contraceptive, how many days within this period can be safely recommended as "infertile"? How can this be ascertained correctly from the temperature chart?

REPLY.—During the normal menstrual cycle, the curve of basal body temperature is biphasic. The temperature is lower in the first half of the cycle than in the second. At the time of ovulation, a slight fall of temperature occurs, followed by a rise of two-fifths to three-fifths of a degree Fahrenheit. A fall of temperature occurs two to three days before the onset of the next menstrual period, but if conception has occurred the temperature does not fall, but continues to rise. In calculating the "safe" or infertile period during the cycle, certain facts have to be considered. It is important for an individual woman to keep graphs of basal body temperature for two to three cycles. On the pattern obtained, it should be possible to note the time of ovulation in each cycle. It must be remembered that any temporary constitutional disturbance, such as a sore throat, may modify the chart, and such occurrences should be noted. Having ascertained the time of ovulation, the ovum is probably capable of being fertilized for two days after. The "safe period" thus begins two to three days after ovulation, and conception should be impossible until the next ovulation. The "safe period", especially when checked by a basal temperature graph, is reasonably reliable as a method of birth control. Fallacies do arise, however. It is possible that in certain women, ovulation may take place more than once in a single menstrual cycle.

JOSEPHINE BARNES, D.M., F.R.C.S., M.R.C.O.G.

Analgesia in Labour

QUERY.—What analgesic drugs are recommended in (a) the first stage of labour, and (b) the second stage of labour in primiparæ and multiparæ?

REPLY.—(a) The amount of help needed from drugs by patients in labour varies considerably according to the type of the pains and the

end-products, when the infant is katabolizing its own reserves. This common high blood urea figure in marasmus does not signify uræmia in the form of kidney disease. The plasma proteins (normal 6.5 to 7 mgm. per 100 c.cm.) often fall to a low figure. Hence the value of whole blood or plasma transfusion. With fall of fluid content in dehydration, higher serum chlorides (normal 550 to 620 per 100 c.cm.) and sodium (normal 330 mgm. per 100 c.cm.), and a high hæmoglobin percentage due to oligæmia appear. With improved hydration, if the chlorides remain high, acidosis is indicated, and a transfusion of Hartmann's, or of 1/6 molar lactate (a solution of sodium lactate, metabolized in the liver to sodium bicarbonate) is indicated, in place of one of sodium chloride or saline solution. If on hydration the serum potassium is reduced (normal 20 mgm. per 100 c.cm.) and acidosis suspected, potassium chloride, 1 gm. added to the drip per twenty-four hours, may help. The plasma bicarbonates, 54 vol. of CO_2 per cent., or CO_2 combining power, indicate by plus or minus a tendency to alkalosis or acidosis.

W. G. WYLLIE, M.D., F.R.C.P.

NOTES AND QUERIES

Subacute Bacterial Endocarditis

QUERY.—What is the criterion of cure in a case of subacute bacterial endocarditis treated with sulphapyridine and a full course of penicillin, i.e., for three weeks continuously, dosage being 50,000 units every three hours? The patient is now free from all subjective signs and is able to carry on his profession as a teacher. He occasionally gets a rise of temperature, especially in the evening, to about 100°F . (37.8°C .), although there is practically no discomfort due to this and his work does not appear to affect it, i.e., absolute rest seldom brings it down and exercise does not increase it. There is still a systolic murmur at the apex. What are the chances of a recurrence?

REPLY.—When a patient is "cured", he loses all evidence of subacute bacterial endocarditis except for signs of valvular damage and, sometimes, the presence of red cells in the urine; there is no fever, weight is regained, anæmia is repaired, erythrocyte sedimentation rate becomes normal, and, of course, blood cultures are negative. Unfortunately some patients, who appear to be cured, die later from heart failure or some other cause, and are found to have colonies of apparently live organisms in their heart valves. The significance of this is not clear, but it is possible that clinical "cure" does not necessarily mean that the infection has been entirely eliminated.

The fever in the present case may be due to an apical abscess or to another as yet undiscovered septic focus, or there may be subacute rheumatic fever. But if these have been excluded, the patient should have repeated blood cultures, some anaerobically. If other signs of subacute bacterial endocarditis return, even if blood cultures are negative, the patient should

be given a second course of penicillin, this time 250,000 units, every three hours for six weeks. The course of treatment that this patient received is now known to be too short, and carries a relapse rate of 20 per cent. in previously untreated cases. If the patient is in fact cured, the chance of recurrence is about 2 per cent. per annum. The results of penicillin in subacute bacterial endocarditis are not as good as they might be; in particular, the high death rate after apparent cure is disappointing. That is why, in this country, practitioners have been asked to send their cases to one of the nine centres where this problem is being specially investigated. (*See Christie, R. V., Brit. Med. J., 1948, i, 1.*)

PROFESSOR R. V. CHRISTIE, M.D., D.Sc., F.R.C.P.

Alkali Therapy in Peptic Ulcer

QUERY.—I should be grateful for a reply to the following questions which crop up in connexion with the treatment of peptic ulcer with a constant alkaline drip: (1) Is the ideal to produce absence of free HCl or to ensure a minimum pH? If so, what pH? (2) In guarding against alkalosis, is there any short cut to carrying out estimations of the alkali reserve? In what sense is the pH of urine any guide to the presence of alkalosis?

REPLY.—(1) The object of treatment with alkalis in peptic ulcer is to ensure that the reaction of fluid bathing the ulcer is at the optimum for ordinary tissue, that is at a pH of 7.4 which is near neutrality. Experiments have been carried out with various alkalis to determine their neutralizing effect. When sodium bicarbonate, magnesium carbonate or magnesium trisilicate is added in excess to an 0.3 per cent. solution of hydrochloric acid, the pH

of the resulting mixture lies between 7 and 9, that is, on the alkaline side of neutrality. In the case of magnesium oxide it will rise as high as 10, whilst bismuth carbonate will produce a pH of about 4, which is well on the acid side. Thus when administering alkalis the idea is to give sufficient to maintain the gastric contents more or less neutral in reaction, but in practice all that can be done is to ensure that the gastric contents are not highly acid. This may best be done by using a neutralizing agent such as magnesium trisilicate which, being practically insoluble in alkaline solutions, will not tend to produce alkalosis, even when present in excess, as some other antacids do. If magnesium trisilicate is actually present in excess over the acid secreted by the stomach, the pH of the stomach contents will be just on the alkaline side of neutrality. The inquirer makes an error in speaking of a "minimum pH" when he means, I believe, absolute neutrality or a pH of 7. A "minimum pH" would represent a highly acid solution.

(2) There is no short cut to carrying out estimations of the alkali reserve. It is true that the urine in a case of alkalosis which results from the excessive ingestion of alkali is always alkaline. If the freshly passed urine from a patient taking alkalis is acid to phenol red (i.e., it is of a pH of less than 6) the patient cannot be suffering from alkalosis of such cause, but no further conclusion could be drawn.

W. N. MANN, M.D., F.R.C.P.

Habitual Abortion

QUERY.—What should be the management of pregnancy in a woman of thirty-eight, who has had abortions at two and three months? Since the one six years ago she has had a dilatation and curetting. Have progesterin and vitamin E any place in an effort to carry her over the danger period at the times of the missed menses?

REPLY.—Already six years have elapsed since the last pregnancy and the case warrants a full investigation for the delay in conception. Both husband and wife need to be fully examined. Tubal patency should be tested. The examination should include renal function tests. Vitamin E has no place in treatment. As for progesterone, here one is on more controversial ground. Abortion can occur even when progesterone is present in adequate amounts, as shown by estimation of pregnanediol in the urine. If the excretion of this substance is low the implantation of progesterone will probably not do any harm. On the other hand, if it is high such treatment may induce an abortion. The subject of habitual abortion is still very confused. The simplest, cheapest, and sometimes most effective

tive treatment is absolute rest in bed during the early months. Barbiturates should be given, but not morphine.

W. C. W. NIXON, M.D., F.R.C.S., F.R.C.O.G.

The "Safe Period" and Birth Control
 QUERY.—In the issue of *The Practitioner* for March 1948, under the query "Temperature Charting in Relation to the Safe Period", there is no mention as to the safety of the period "after menstruation to the next ovulation". I shall be grateful if you could let me know what is the safe period. For those who do not like to use any contraceptive, how many days within this period can be safely recommended as "infertile"? How can this be ascertained correctly from the temperature chart?

REPLY.—During the normal menstrual cycle, the curve of basal body temperature is biphasic. The temperature is lower in the first half of the cycle than in the second. At the time of ovulation, a slight fall of temperature occurs, followed by a rise of two-fifths to three-fifths of a degree Fahrenheit. A fall of temperature occurs two to three days before the onset of the next menstrual period, but if conception has occurred the temperature does not fall, but continues to rise. In calculating the "safe" or infertile period during the cycle, certain facts have to be considered. It is important for an individual woman to keep graphs of basal body temperature for two to three cycles. On the pattern obtained, it should be possible to note the time of ovulation in each cycle. It must be remembered that any temporary constitutional disturbance, such as a sore throat, may modify the chart, and such occurrences should be noted. Having ascertained the time of ovulation, the ovum is probably capable of being fertilized for two days after. The "safe period" thus begins two to three days after ovulation, and conception should be impossible until the next ovulation. The "safe period", especially when checked by a basal temperature graph, is reasonably reliable as a method of birth control. Fallacies do arise, however. It is possible that in certain women, ovulation may take place more than once in a single menstrual cycle.

JOSEPHINE BARNES, D.M., F.R.C.S., M.R.C.O.G.

Analgesia in Labour

QUERY.—What analgesic drugs are recommended in (a) the first stage of labour, and (b) the second stage of labour in primiparæ and multiparæ?

REPLY.—(a) The amount of help needed from drugs by patients in labour varies considerably according to the type of the pains and the

attitude of the patient towards them. Early in labour the old-fashioned chloral and bromide mixture, 30 grains (2 gm.) of each by mouth, is useful. When the first stage is well established morphine $\frac{1}{2}$ or $\frac{1}{4}$ of a grain (11 or 16 mgm.) and hyoscyine $\frac{1}{150}$ of a grain (0.43 mgm.) by subcutaneous injection (the os being 2 fingers dilated) is one of the best combinations to give and will carry the patient well into the second stage. Nowadays pethidine is used extensively as an alternative and is effective. Dosage 100 mgm. intramuscularly. This can be repeated in an hour or two and then two- or four-hourly; maximum dose 400 mgm. If the first stage is very prolonged paraldehyde, 14 to 21 c.cm. in olive oil or liquid paraffin, 4 to 6 ounces (114 to 170 c.cm.), administered by the rectum is good, as is also a combination of pethidine, 50 to 100 mgm. by injection, and seconal, $1\frac{1}{2}$ grains (0.1 gm.) orally. All these drugs are for use in the first stage and should not be used if the birth of the child is expected in an hour or two.

(b) In the second stage, analgesia is best obtained by some type of gas-oxygen or gas-air mixture (e.g. Moir's type of Minnitt's apparatus) or by an anæsthetic. Trilene by Freedman's inhaler is good but should not be used in patients with toxæmia or cardiac disease. This last, or a little chloroform or ether on a mask, will serve for delivery of the head. Great care is necessary of patients in prolonged labour, as their metabolism alters, and also the dangers of anæsthesia must be mentioned because of the tendency of patients in labour to have delayed emptying of the stomach, and the risk therefore of vomiting.

KENNETH BOWES, M.S., F.R.C.S., F.R.C.O.G.

The Treatment of Syphilis in Pregnancy

QUERY.—What is the correct method of treating syphilis in the pregnant woman?

REPLY.—Treatment of the pregnant woman who is suffering from syphilis is designed to protect the fœtus from prenatal syphilis, and to cure the mother. The first aim is best attained by adequate dosage of penicillin. All the evidence points to the fact that this will protect the fœtus in 98 per cent. of the cases, irrespective of the stage of infection in the mother or the degree to which pregnancy is advanced. Dosage should be 2.4 to 4 million units of commercial sodium penicillin, dissolved in sterile distilled water or normal saline, given intramuscularly in divided doses three-hourly day and night, during a period of seven to fifteen days. The following systems of treatment have proved satisfactory:—

(1) 40,000 units three-hourly for 60 doses = 2,400,000 units in 7½ days.

(2) 40,000 units three-hourly for 85 doses = 3,400,000 units in 10½ days.

If admission to hospital is impossible, equally good results can probably be obtained by giving calcium penicillin suspended in arachis oil and 4.8 per cent. beeswax: 250,000 units twice daily for 8 days = 4,000,000 units. For cure of the mother this treatment alone may be adequate, but if the patient has early syphilis it is customary in this country to supplement the penicillin by giving a full course of arsenic and bismuth in weekly injections for ten weeks as follows:—

1st week: Neoarsphenamine, 0.45 gm. intravenously. Suspension of bismuth metal, 0.3 gm. intramuscularly.
2nd to 10th week: Neoarsphenamine, 0.6 gm. intravenously. Suspension of bismuth metal, 0.3 gm. intramuscularly.

If the patient has late syphilis she must, of course, be fully investigated to ascertain the extent of the damage. In such event it may be considered advisable to avoid arsenic and rely upon penicillin alone, or the combination of penicillin and bismuth. Care in starting treatment is important to avoid exacerbation of the condition, as part of the so-called Jarisch-Herxheimer reaction. Prolonged and careful observation and testing are necessary after treatment is finished. It is customary to advise further treatment with penicillin in subsequent pregnancies, even though the patient appears to be cured.

AMBROSE KING, M.B., F.R.C.S.

Unilateral Disturbance of the Autonomic Nervous System

QUERY.—I shall be glad of advice on the treatment of the following case. A woman aged fifty has weak heart beats, chronic bronchitis, intermittent "slight inflammation of the kidneys", blood pressure 140/80 mm. Hg. About four years ago she began to feel (and by touch also) that her left hand was hotter than the right and later that the left arm was hotter than the right arm. Gradually she found that the entire left half of her body was hotter than the right, even in cold weather. The left side of the body does not sweat even in hot weather. She is married and has one daughter. The W.R. is negative.

REPLY (from a neurologist).—The local condition is a unilateral disturbance of part of the autonomic nervous system concerned with flushing and sweating, to which reference is made in "Rare Diseases and Some Debatable Subjects" by F. Parkes Weber, second edition, 1947, p. 65. Treatment might be confined to that of the general condition, about which further details should be known. Possibly drugs such as small doses of theominal might be useful for a time.

PRACTICAL NOTES

p-Aminosalicylic Acid in Pulmonary Tuberculosis

A REPORT on the results of *p*-aminosalicylic acid therapy in six cases of pulmonary tuberculosis is given by A. Erdei (*Lancet*, May 22, 1948, i, 791). The drug was used in the form of a sodium salt solution prepared from the crystalline powder, the dosage employed being 12 gm. daily, by mouth, in divided doses three-hourly, one night dose being omitted. Five patients received a sixty-day course, and one a four-week course. With the dosage employed a blood level of 2-5 mgm. per 100 c.cm. was obtained; the urine was loaded with salicylates, and in three cases faint traces were present in the sputum. The most striking result of the treatment was the improvement in the patients' general condition; there was also reduction in the level and swing of the temperature, and in the number of organisms in the sputum. No toxic reactions occurred. The author, who advocates further trials with higher dosage, states that "although *p*-aminosalicylic acid cannot be regarded as a cure for pulmonary tuberculosis, it is very active in the exudative and toxic forms . . . it may also have a beneficial influence on tuberculosis of the urinary tract". In a comment by W. E. Snell, Physician-Superintendent of Colindale Hospital, it is stated that although "the duration of treatment has been too short for any real conclusion to be formed . . . the improvement in these few cases is sufficient to warrant an intensive trial of this treatment . . ." It is of interest to note in this connexion an article on the subject by L. Ragaz (*Schweizerische Medizinische Wochenschrift*, April 10, 1948, 78, 332), in which rapid improvement in 60-70 per cent. of cases of pulmonary tuberculosis following *p*-aminosalicylic acid therapy is recorded: improvement in general condition, fall in temperature, increase in weight, decrease in blood sedimentation rate, and also in the number of bacilli in the sputum. The dosage used was 10-15 gm. daily for a week, with an alternating week free of treatment, the duration of treatment being for several months. A case of tuberculosis of the kidneys was negative for tubercle bacilli in two weeks, and symptom-free in eleven weeks after institution of *p*-aminosalicylic therapy. This author also advocates the carrying out of further therapeutic trials.

of *Dermatology and Syphilology*, January 1948, 57, 57) consider it to be an effective therapeutic agent. It is also inexpensive and is safe to use if reasonable care is exercised. Contact with fire must be avoided. It is applied by means of a wooden applicator covered with cotton-wool. The length of time for which it is applied to the skin depends upon the extent and depth of the lesion, varying from 15 seconds to 1½ minutes. The time required in any one case is soon learned from experience. There is always a certain amount of pain. In three to twenty-four hours a vesicle or bulla develops at the site of application. The conditions which have been treated successfully in this way include warts, hæmangiomas, leucoplakia, seborrhæic keratoses and senile keratoses. Among the advantages claimed for this form of treatment are: (a) it is easier to apply than solid carbon dioxide; (b) simplicity of use; (c) scarring is minimal and of the soft variety; (d) keloids are not produced in patients who develop keloids after other forms of trauma.

Pyribenzamine in Angina Pectoris

AN interesting case of a fifty-one-year-old physician who had suffered from angina pectoris for three years, and whose anginal pain disappeared following treatment with pyribenzamine for a contact dermatitis, is recorded by J. McEachern (*Canadian Medical Association Journal*, May 1948, 58, 503). The patient, who was unable to walk "a block" without substernal distress, whose blood pressure was usually 160/100 and electrocardiograms showed moderate evidence of hypertensive heart disease, was prescribed a dose of 50 mgm. pyribenzamine to be taken during breakfast and lunch and at bedtime. A few days later the patient realized he no longer experienced anginal pain. The pyribenzamine was continued, in dosage of 50 mgm. at breakfast and 25 mgm. at lunch, and with one exception, following exposure to cold and exertion, there was no recurrence of pain: "The coronary claudication time has been doubled. . . . Not only can he walk farther but . . . twice as fast". Following this result pyribenzamine was given to eight patients with angina with instructions to study their exercise tolerance; seven reported definite improvement. Further careful studies on a series of cases are being undertaken.

Liquid Oxygen in Dermatology

HAVING used liquid oxygen, which is 175° F. colder than solid carbon dioxide, in more than 1000 cases, R. L. Kile and A. L. Welsh (*Archives*

A New Remedy for Headache

A REPORT on the clinical observations on the use of E.C.110 (ergotamine tartrate 1 part; caffeine 100 parts—Sandoz) is given by B. T.

Horton, R. Ryan and J. L. Reynolds (*Proceedings of the Staff Meetings of the Mayo Clinic*, March 3, 1948, 23, 105). The report concerns fifty-five patients who attended the clinic for headache. The cases included migraine (25), histaminic cephalgia (14), tension headache (11), arteriosclerotic headache (2), and pain in the face (3). The average dose was two tablets (each containing 1 mgm. ergotamine tartrate, and 100 mgm. caffeine) at the onset of headache. Excellent results (i.e., complete relief in from 20 min. to 4 hr.) were obtained in 16 of the cases of migraine, good results in 6, and poor in 3. In the histaminic cephalgia group, excellent results in 10, good in 3, and poor in 1. In the tension group the results were excellent in 5, good in 3, and poor in 3. In the arteriosclerotic group, good 1, and poor 1. The results were poor in all three cases of atypical pain in the face. Toxic symptoms occurred in only three cases in which two to four tablets were administered; these symptoms consisted of slight giddiness, nausea and abdominal distress. In one case, however, in which a man took six tablets daily for twenty days, severe gastro-enteritis occurred, with muscular cramps and urinary retention.

Intramuscular Copper Therapy in Chronic Inflammatory Rheumatism

USING cupro-oxyquinoline sulphonate of methylamine in a 10 per cent. aqueous solution, fifty-five cases of chronic inflammatory rheumatism have been treated by J. Forestier, F. Jacqueline and S. Lenoir (*Presse Médicale*, May 15, 1948, 56, 351). The dosage employed was 0.5 gm. per injection, twice weekly, up to a total of 6 or 9 gm., i.e. twelve or eighteen injections, according to the severity of the case. In order to prevent pain from the injection, in some cases 2 c.cm. of 2 per cent. novocain or scurocain were added in the syringe. Further series of treatment were given after four weeks, six weeks, and two months. Excellent results were obtained in 13 cases; good results in 26; moderate in 7; failures 9. As regards toxic reactions, there were three cases of skin affection, and in some cases there was slight nausea and indigestion. One patient who developed severe albuminuria after gold therapy not only tolerated the copper injections well, but also while receiving injections showed a decreased albuminuria. Of 20 cases of chronic progressive polyarthritis, the sedimentation rate returned to normal in 7, and showed a marked decrease in 7. The series included three cases of chronic polyarticular gout, all of which responded well to treatment without any disturbance of renal function.

Mercurial Discoloration of the Eyelids

ATTENTION is drawn by M. Wheeler (*American Journal of Ophthalmology*, April 1948, 31, 441) to the pigmentation of the eyelids which may occasionally follow the prolonged local use of mercurial ointments. He gives details of five cases in which this has occurred. In all five cases an ophthalmic ointment containing mercury (yellow oxide or ammoniated) had been used daily for periods ranging from four to twenty-three years. In only one case was the pigmentation marked: a dirty grey colour of the skin of both lower eyelids and of the lower 15 mm. of the upper lids. Examination by slit lamp revealed "a homogenous grey coat to the skin; the pigmentation extended on to the lid margins as granules more brownish than grey". In three others the discoloration—a faint grey, slightly greasy appearance of the eyelids—had not been noticed by the patients themselves and was only noted on routine examination. In no case was there any pigmentation of the conjunctiva. Treatment is seldom indicated; all that is required is cessation of the use of the mercurial ointment. This is followed by fading of the discoloration.

Penicillin in the Treatment of Neurosyphilis

TWENTY-FOUR cases of neurosyphilis, including dementia paralytica (8), tabes (5), optic atrophy (2), and meningo-vascular syphilis (9) have been treated by intramuscular injections of penicillin by J. Purdon Martin (*British Medical Journal*, May 15, 1948, i, 922). After the first day of treatment, on which the dosage of penicillin was small, 60,000 units were given three-hourly until a total of 5 million units was reached. The dosage on the first day was 15,000 units t.d.s., or 10,000 units hourly, orders being given that administration should stop if the patient complained or seemed upset. No untoward reactions occurred, however. In the first group (dementia paralytica) all the patients showed clinical improvement, and all were working after observation of six to twelve months; in most instances the cerebrospinal fluid became negative in about a year, thus indicating arrest of the disease. In group two (tabes) all patients showed subjective improvement with diminution of lightning pains. In group three (optic atrophy) one patient was blind in the right eye and had diminishing vision in the left. After treatment vision in the left eye, which was at first 6/12, recovered to a little better than 6/6, and there was slight recovery of sight in the right eye. In the second case deterioration of vision was arrested after two courses of penicillin

therapy. In group four (meningo-vascular syphilis) there was marked improvement in five cases, including three with cerebral syphilis; moderate improvement in three; in one (generalized vascular disease with high blood pressure) little improvement could be expected. In conclusion, the author states: "Penicillin alone is sufficient in most cases of neuro-syphilis", and "if (with the possible exception of acute cases of G.P.I.) the patient can be kept under observation after treatment and penicillin repeated if necessary, malaria will seldom be called for, and the risk of it will seldom be justified".

Night Cramps of the Extremities

NIGHT cramps of the extremities appear to be due to some end-product of metabolism, as in diabetes, or to poor elimination of normal end-products of muscle metabolism, as in venous stasis due to varicose veins, pregnancy, or following deep venous occlusion. Increased muscular activity favours the development of night cramps in the rest following such activity. These facts are pointed out by H. K. Moss and L. G. Herrmann (*American Heart Journal*, March 1948, 35, 403) who have observed the results of quinine sulphate therapy in twenty patients. Quinine sulphate, 3 grains (0.2 gm.), a placebo, and prostigmine bromide, 7.5 to 15.0 mgm., were prepared in identical capsules, the patients being started either with quinine sulphate or the placebo; if the former, the placebo was substituted as soon as relief from night cramps was noted. The initial dosage of quinine sulphate was 3 grains (0.2 gm.) after each meal. Subsequently 3 grains (0.2 gm.) of quinine sulphate were given after supper and at bedtime. Relief was usually obtained on the first or second night, often complete, although in some cases mild or less frequent cramps occurred for some days. In many cases repeated alternations with a placebo were possible; eventually relief of muscle cramps persisted without medication. No alteration in the frequency and intensity of night cramps was observed in those patients who received prostigmine bromide before the quinine therapy, and in only two patients did prostigmine induce muscle cramps after relief by quinine. Beneficial effects of prostigmine, however, were (1) peripheral vasodilatation in arteriosclerotic patients; (2) one patient noted marked improvement in intermittent claudication; (3) increased motility in arthritic joints. Subsequently, prostigmine was used with benefit in a group of patients suffering from osteoarthritis. In conclusion, the authors state that "prostigmine, the supposed pharmacologic antagonist of

quinine, failed to increase the intensity or frequency of night cramps when administered in doses sufficient to produce the vasodilating effect of the drug".

Benzedrine in Enuresis

ENURESIS is attributed to disturbance during sleep of the centres controlling the innervation of the bladder. In the normal bladder there are two antagonistic groups of nerves: one stimulates contraction of the muscle of the body and fundus, and increases the tone of the detrusor fibres; the other decreases the tone of the muscle fibres of the trigone and of the neck of the bladder. These normally act synergistically. In enuresis the action of the first group is stronger, and the result is involuntary micturition. When the tone of the detrusor fibres is increased, A. A. Puntel (*Revista de Medicina y Ciencias Afines*, November-December 1947, 9, 720-21) finds small doses of benzedrine effective, beginning with 5 to 10 mgm. by mouth. A case is reported of an unmarried girl of nineteen, who had suffered from enuresis since infancy. Striking improvement was noted after the first dose, and there was complete cure after two months of treatment.

Tinted Lenses

THE following excerpts are taken from an article by Alfred Cowan, which has been adopted by the Council on Physical Medicine of the American Medical Association (*Journal of the American Medical Association*, April 24, 1948, 136, 1098):—"Unless the eyes are sick or abnormally sensitive, dark glasses are indicated only in the presence of extraordinary, excessive or misdirected light. Healthy, properly corrected eyes should be well able to tolerate bright sunlight unless it is reflected directly into the eyes by water, snow, sand or the like". . . . "On the occasions when protection is necessary the glasses should be dark enough to absorb from 60 to 75 per cent. of the light and they should be colourless—smoke or grey". . . . "Tinted lenses should not be worn indoors under properly placed artificial light and never outdoors at night. They are dangerous for night driving. . . . The sense of ocular fatigue after day driving is more often due to uncorrected or improperly corrected errors of refraction or of muscle balance than to the bright light". . . . "Despite the fantastic, absurd and untrue claims of the manufacturers of certain tinted glasses, the lighter shades of coloured glass—tints that are hardly perceptible—offer little more protection against glare than clear glass".

REVIEWS OF BOOKS

Oral and Dental Diseases. BY HUBERT H. STONES, M.D., M.D.S., F.D.S.R.C.S. Edinburgh: E. & S. Livingstone Ltd., 1948.

Pp. xix and 896. Figures 926. Price 90s.

THE rapid advance that has taken place in knowledge of the etiology and pathology of oral disease has led to the publication of a multiplicity of textbooks in an endeavour by authors to present the latest facts. They mainly deal, however, with a limited field, such as parodontia, orthodontia, or pathology, and are written in a detailed way more suited to the specialist than to the student or general practitioner. Professor Stones has filled an urgent need by presenting in one textbook the essential details and facts of the whole field of oral and dental disease. The approach, generally, is from a medical angle and the author avoids the tendency, so often displayed in dental textbooks, of treating dental disease as something occurring independently from the rest of the body, either as regards cause or effect. The physiology of the tissue involved is fully dealt with and it is from that sound basis that a study of the pathological conditions are developed. A full description is given of recent research work, including much of the author's own original investigations that have a bearing on the etiology or treatment of the various conditions: this adds much to the value and interest of the book. The application of research findings to clinical practice naturally requires considerable experience, and it would have been an advantage, in the interests of students, if the author had drawn more definite conclusions. The book is abundantly illustrated by excellent photographs and drawings and the publishers are to be congratulated upon a production reminiscent of a pre-war edition. It will, undoubtedly, appeal to medical practitioners, who will find in it much to interest them, as well as being an excellent book for reference. It is written in a concise and clear way which makes reading a pleasure and grips the attention. Advanced students and research workers will find a useful bibliography at the end of each chapter.

Tuberculosis in Young Adults. BY MARC DANIELS, M.D., D.P.H., FRANK RIDEHALGH, M.B., B.CHIR., M.R.C.P., V. H. SPRINGETT, M.B., B.S., and I. M. HALL, M.B., B.S., M.R.C.P. London: H. K. Lewis & Co. Ltd., 1948. Pp. xvi and 227. Plates 58. Figures 22. Price 30s.

WORKING under the ægis of the Royal College of Physicians of London, the main object of the

Prophit Tuberculosis Survey has been "to try to determine whether it is possible to pick out those persons or group of persons most likely to develop tuberculosis". The present volume is the report of the survey for the period 1939-45, and is based upon a study of 10,000 presumably healthy young adults drawn from five sections of the community: (a) contacts of tuberculous subjects; (b) medical students; (c) hospital nurses; (d) naval boys; (e) controls. The two main methods of investigation were the Mantoux skin test and radiological examination of the chest. Like so many carefully planned pre-1939 projects, the survey was seriously affected by the exigencies of war, but in spite of this the present report presents a wealth of carefully acquired and controlled data which will prove of value in the control of tuberculosis in man. It is no slur on the ability of those responsible for the survey that the report adds little that is fresh to the knowledge of a complex subject: it is valuable in providing accurate data capable of statistical analysis, on problems such as the real significance of a positive tuberculin reaction, Mantoux reversion and Mantoux conversion. Many such surveys have been conducted in other countries, notably Scandinavia, but this is the first time the problem has been tackled on an adequate scale in this country. To attempt to summarize the findings would be impossible, but it can safely be said that this is a report that must be carefully studied by all concerned with the care of the tuberculous, and, perhaps more important still, by all concerned with the medical welfare of the young adult, particularly nurses and medical students.

Private Enterprise or Government in Medicine. BY L. H. BAUER, A.B., M.D., F.A.C.P. Springfield, Illinois: Charles C Thomas; Oxford: Blackwell Scientific Publications, 1948. Pp. ix and 201. Price 25s.

"IN all that the people can individually do as well for themselves the government ought not to interfere". This quotation from Abraham Lincoln, which is inscribed on the dust cover of this book, epitomizes the thesis so vigorously propounded by the author. Dr. Bauer, who is a member of the board of trustees of the American Medical Association, is an able polemicist and does not pull his punches. Written primarily for the American public, it provides a comprehensive review of the present state of the practice of medicine in the United States, and then dis-

cusses the programmes of reform which have been advanced by the American Medical Association. Compulsory health insurance is the *bête-noir* of the Association, and Dr. Bauer includes in his book a chapter reviewing compulsory health insurance in other countries. That this review is anything but favourable to the system is well shown by the following two quotations from the section dealing with Great Britain: "In twenty years of compulsory insurance in England, the morbidity rate among the insured class doubled". Then in reference to the National Health Act: "The bill was enacted and a backward step was taken. The art of medicine will disappear and medical science will become strangled in bureaucratic red tape". The American way of living may be different from ours, but there will be many who will read this fascinating book with pangs of regret for the old order that is now gradually passing from our midst. Here is the quintessence of that sturdy individualism which has stood us so well in the past, but which apparently is now considered too old-fashioned for this modern age of ideological rationalization.

Psychiatric Examination of the School Child. BY MURIEL BARTON HALL, M.D.
London: Edward Arnold & Co., 1947.
Pp. viii and 368. Price 15s.

THIS book forms an excellent introduction to the study of the school child. The author has had a wide experience of children from different social classes. She has worked with them during a period which has included a trade depression, war and demobilization. The book covers such subjects as the backward child, nervous habits, e.g. enuresis, stammering, and personality disorders, e.g. temper tantrums, lying and pilfering, and the early manifestations of the adult forms of neurosis and psychosis. The social and legal aspects are fully discussed, as well as the art of writing reports. Some 230 authors are quoted. Written in a pleasing style and easy to read, it will well repay study by practitioners and others who work with children.

NEW EDITIONS

Textbook of Public Health, by W. M. Frazer, O.B.E., M.D., M.Sc., D.P.H., and C. O. Stallybrass, M.D., D.P.H., in its twelfth edition (E. & S. Livingstone Ltd., 30s.) gives details of new legislation since the appearance of the previous edition in 1946: the National Health Service Act, the National Insurance Act, the Family Allowance Act, and the National Insurance (Industrial Injuries) Act. The work, which is too well known to call for detailed comment, covers the ground for the Certificate and

Diploma in Public Health and also the Diploma of Tropical Medicine and Hygiene.

Major Endocrine Disorders, by S. Leonard Simpson, M.D., F.R.C.P., in its second edition (Oxford University Press, 42s.) contains a new section on alloxan diabetes; the use of stilbestrol in prostatic carcinoma is included, as also pregnanediol estimation in pregnancy, the use of progesterone in threatened abortion, radio-active iodine in thyrotoxicosis, and testosterone propionate in eunuchoidism—these are but a few of the many additions to a work which contributes much to the study and practice of endocrinology.

THE sixth edition of *Emergency Surgery*, Part 1, by Hamilton Bailey, F.R.C.S. (John Wright & Sons Ltd., 21s.) opens with chapters on cannulization for infusion and transfusion, and on blood transfusion. Both chapters are richly illustrated. Anaesthesia for urgent surgery, and methods of dealing with impending death under anaesthesia are dealt with before the author passes on to abdominal surgery.

New sections on the use of the antibiotics and the sulphonamides have been included in *Minor Surgery*, by Frederick Christopher, M.D., B.S., F.A.C.S., in its sixth edition (W. B. Saunders Co. Ltd., 60s.), and revision of the sections on thrombophlebitis and phlebothrombosis has been carried out to incorporate anticoagulant therapy. The new edition is generously illustrated (595 figures) and there is a good bibliography.

HURCHISON'S *Food and the Principles of Dietetics*, revised by Professor V. H. Mottram, and George Graham, M.D., F.R.C.P., in its tenth edition (Edward Arnold & Co., 21s.) has been largely rewritten. Part 1, on diet in normal life, is almost entirely new. Although diet is still overshadowed by post-war conditions and controls which limit many dietetic schemes, this work contains much valuable information.

Modern Psychiatry in Practice, by W. Lindesay Neustatter, M.D., M.R.C.P., B.Sc., in its second edition (J. & A. Churchill, Ltd., 12s. 6d.) contains two new chapters, on psychopathy and neuropsychiatry, respectively. On the basis of the more general usage of the term, the word "psychiatry" has been substituted for "psychology" in the title of the book.

Restoration Exercises for Women: Embodying Stand Up and Slim Down, by Ettie Rout, in its ninth edition (Wm. Heinemann [Medical Books] Ltd., 7s. 6d.) In addition to prenatal, postnatal, postoperative, and everyday exercises for women, a chapter on food selection for constipation and obesity is included.

NOTES AND PREPARATIONS

NEW PREPARATIONS

"NEO-EPININE" brand isopropyl-noradrenaline, a new compound of isopropyl-adrenaline for use in the treatment of asthma, is issued in the form of tablets for sublingual administration, in bottles of 25 tablets of 20 mgm., price 3s. 6d. A spray solution will shortly be issued. The manufacturers are Burroughs Wellcome & Co., 183-193 Euston Road, London, N.W.1.

STERAMIDE-AG. (sulphacetamide soluble 30 per cent., silver vitellinate 5 per cent.) has been prepared for the local treatment of ocular and nasopharyngeal infections. It is issued in pipette bottles of 25 c.cm., price 6s., by Ward, Blenkinsop & Co., Ltd., 6 Henrietta Place, London, W.1.

T.S.R. (brand of travel sickness remedy) is a combination of scopolamine, atropine, and phenobarbitone, each tablet containing scopolamine hydrobromide $\frac{1}{300}$ grain (0.23 mgm.), atropine sulphate $\frac{1}{400}$ grain (0.16 mgm.), and phenobarbitone $\frac{1}{2}$ grain (32 mgm.). It has been prepared for use in the prevention of motion sickness, by Bayer Products Ltd., Africa House, Kingway, London, W.C.2, by whom it is issued in packings of 10 and 50 tablets.

D.C.L. YEAST AND YEAST PRODUCTS
THIS is the title of a booklet produced by the Distillers Company Ltd., 8-12 Torphichen Street, Edinburgh, 3, in which the many uses of D.C.L. yeast and details of its production are admirably described by W. G. Bennett, D.Sc., F.R.I.C. A copy of the booklet and samples can be obtained on application to the manufacturers.

"INNERAZE" SHOES FOR FLAT FEET
THE Inneraze shoe for children has been devised for the treatment of flat foot, with an in-built wedging between the inner and outer sole, which is an integral part of the shoe, thus avoiding shoe distortion and consequent uneven wear. The film "Progress Afoot" describes the construction of the Inneraze shoe which is supplied on prescription only, by Messrs. Southall of Norwich, the manufacturers of the "Start-Rite" shoe.

THE FLORENCE NIGHTINGALE HOSPITAL

THE centenary of this hospital, founded by Miss Nightingale in 1848, coincides this year with the announcement of its exemption from State control by the Minister of Health. An illustrated pamphlet, entitled "One Hundred Years Ago", by Violet A. Miles, tells the story of the foundation of the hospital "for the relief and comfort during temporary illness of invalid

gentlewomen". This tradition has been nobly carried out. Copies of the pamphlet can be obtained from the Secretary, Florence Nightingale Hospital, Lisson Grove, London, N.W.1.

PUBLICATIONS

An Index to Modern Remedies, by William Mair, F.R.S.E., F.C.S., M.P.S., fourth series (The Scottish Chemist, 3s.) contains useful lists of chemical substances with their official names, proprietary forms, chemical constitution, and therapeutic applications—a new innovation which will be much appreciated by practitioners, who will find this carefully compiled publication of much practical value.

Handbook of Communicable Diseases for the Use of Medical Officers of Schools, in its eleventh edition (J. & A. Churchill Ltd., 5s.) is compiled by the Medical Officers of Schools Association, is presented in a new format based on that used in the booklet on the subject issued by the American Public Health Association.

"The American Lecture Series", published by Charles C Thomas, Springfield, Illinois, and in England by the Blackwell Scientific Publications Ltd., Oxford, are modern guides to different branches of medicine and science, the authors of which are foremost authorities on their various subjects. The monographs are most attractively produced at prices ranging from 4s. 6d. to 12s. 6d. Full particulars can be obtained from the Blackwell Scientific Publications Ltd., 48 Broad Street, Oxford.

PUBLISHERS CATALOGUES

THE 1948 Catalogue of Medical Books, published by E. & S. Livingstone Ltd., of Edinburgh, has just been issued, and a copy can be obtained on application to 16 and 17 Teviot Place, Edinburgh, 1, or to the London Office at 45 Lincoln's Inn Fields, W.C.2.

Blackwell Scientific Publications 1948 Complete Catalogue, comprising 187 works on medical subjects, is available on application to the publishers, 48 Broad Street, Oxford.

EDITORIAL ANNOUNCEMENT

DR. W. N. MANN, M.D., F.R.C.P., Assistant Physician, Guy's Hospital, has been appointed to the Editorial Board of *The Practitioner*.

Binding Cases for Volume 160 (January-June 1948) in green cloth with gilt lettering are now available, price 4s. post free, from the Publishing Department, *The Practitioner*, 5 Bentinck Street, London, W.1.

The contents of the August issue, which will include a symposium on "Thanatology in General Practice", will be found on page lxxiv at the end of the advertisement section.

SIGNS AND SYMPTOMS OF IMPENDING DEATH

By LORD HORDER, G.C.V.O., M.D., F.R.C.P.

Physician in Ordinary to H.M. the King; Consulting Physician, St. Bartholomew's Hospital.

THE first thought in the minds of many readers of *The Practitioner* may well be that the subject of the present symposium is lugubrious and forbidding. Second thoughts will probably confirm the editorial wisdom upon which we have come to rely. "Neither the sun nor death [said the French cynic] can be looked upon with a steady eye". There is the usual exception to prove the rule: familiarity breeds in the doctor the "steady eye" which, as he so often witnesses, the onlooking layman lacks. As for the dying man himself, we rarely find him "looking death in the face" and knowing it is death. He is either very dubious that death is coming to him, or his apperception is so dimmed, whether by weakness or by a merciful physician, that the end of life is a dream-state rather than a true awareness. Even that momentary "lightening before death", which sometimes illumines the dimming consciousness, scarcely serves to give a clear picture, for it yields no true sequence of thought or even of feeling. When a man thinks that death is imminent his anticipation, more often than not, goes unfulfilled. How can it be otherwise, seeing that death comes but once and can therefore not be recognized. A few moments before his death Palmerston is reported to have said: "Die, my dear doctor! That's the last thing I shall do!" It seems uncertain if the noble Viscount's remark expressed a conviction that his physician's prognosis was in error or if he was knowingly adding to those last-word pleasantries which have collected round the death-beds of famous people.

Waking in the night with a sense of "floating away" a bishop reflected "this is death". He forgot, or was unaware of the exhortations of two men who had held his high office some centuries before him, and who thought, the one that a bishop should "die on his legs", the other that he should "die preaching". One bishop asked himself "how should a bishop be found in the morning, being dead?" and decided that the appropriate posture was to lie on his back with his arms crossed over his breast. This he did, and to quote his own words: "Nothing happening, and my arms getting cold I put them back under the coverlet and went to sleep".

A glance at the titles of the articles in this symposium shows that death and dying are part, albeit the final part, of the natural history of disease and therefore one part of the claim which the community has upon the doctor's service: the final part of the natural history of disease but not, of course, the final part of our knowledge of disease. The motto of the old Pathological Society "*nec silet mors*" sufficiently indicates this.

THE DIFFICULTIES OF PROGNOSIS

The question posed to me is one part of what we call "prognosis", notoriously the most difficult assessment that the physician is called upon to make concerning his patient. With so many incalculables determining the act of living this is not surprising. We speak of the immediate prognosis—will the patient live or die of this disease?—and the remote prognosis—if he lives how will his life be affected by this disease? This is the immediate outlook that affects us here, and, in particular, if we think he will die, do we think he will die soon? If we do think this, by what observations do we judge this to be the case?

It may not come amiss to name some observations which, although of great importance in other prognostic relations, do not really give us the answer to our question, although they are often thought to do so. One of these is the fact that the patient is known to be suffering from a lethal disease. A man may be ill with *cancer* of his stomach, may give evidence of secondary deposits scattered about his body, may "look the part" by way of cachexia, and yet the signs of (impending) death may not be written upon his face or upon any other part of him. And so also for the other diseases characterized by the unfortunate word "malignant", one of which, incidentally, (*malignant endocarditis*) has come under therapeutic control.

Another condition which does not give us the answer, but may well suggest it to the unwary, is that his disease makes the patient ill to a degree that seems to render survival impossible.

A *typhoid* patient, having lain unconscious and pulseless for some days, bleeds profusely, narrowing his margin of existence even more. "He cannot possibly live" is not only the comment of untutored friends, it may be that of the doctor also if he be only tutored by his textbook or by a very limited experience. It seems unkind to turn the already sorrowing relatives out of the sick room where they have been summoned by the nurse but, assuming, as he should, that recovery is not impossible, it is his duty so to do in order that he may properly examine the "dying" patient. Typhoid fever may reduce a man's vitality to the merest thread and yet "the blind fury" may still not slit "the thin-spun life".

In *cerebrospinal fever*—granted it would in these days of chemotherapy be an undiagnosed case—a patient lies unconscious, emaciated, apparently dying. Lumbar puncture yields a milky exudate and thecal drainage, by leaving the trocar *in situ* for two or three days, turns the scale and the patient recovers. The story might be repeated with pneumonia, acute

nephritis, congestive heart failure, coronary thrombosis, opium poisoning, and some other morbid states.

Knowledge that the disease is not necessarily lethal, yet is capable of producing an extreme degree of enfeeblement of all functions, stimulates the doctor to continued vigilance and activity. The moral is this, that the mere degree of illness, however extreme, should not be mistaken for the signs of impending death.

This dictum, which I hope I have justified, gives countenance to the attitude adopted by a certain medical officer who was under criticism by two of the Sisters in whose wards he worked: "How do you get on with Dr. X?", said one; "Not at all", said the other, "he won't let the patients die". It is quite certain that many patients die because the doctor thinks they must. The trouble is, he knows too much, or rather he does not know how little he knows.

The state of affairs just described, of not letting people die, must not be confused with the effort to prolong life at the end of an incurable disease. This is quite a different situation. To prolong life in many such cases is, as Samuel Gee remarked, "not prolonging life so much as prolonging the act of dying".

"O' let him pass; he hates him that would upon the rack of this tough world stretch him out longer."

CONCLUSION

If we exclude those extreme degrees of enfeeblement to which I have referred—as I think we must—and if we divest our minds of the knowledge that a man's disease is incurable, then the signs and symptoms of *impending* death are extremely unreliable. Indeed, we know more about the act of dying than we do about the imminence of death itself. And even in the act of dying there may be, there often is, considerable doubt as to the exact moment when death takes place. How often we have watched the dying man, waiting for his life to end, and had to confess that when we thought the last breath had been taken, after an interval which seemed so long, another came—that sudden, sharp gasp with its slow deep expiration. And even that was often not the end, for the end was not an act of breathing at all, but a movement as of swallowing, with a twitch of the mouth or even of the face.

It may well be that the experienced clinician makes observations leading him to conclude that death is impending which he finds it difficult, perhaps impossible, to analyse or describe. I have seen so many experienced observers wrong in their judgment that I am sceptical on this point. So that I have come to believe that the greater a man's experience in this matter the more cautious is he in making a pronouncement. I am not infrequently told that patients died on the very day or at the very hour that I said they would, but on careful inquiry it usually transpires that the story rests more upon the very common human desire that the marvellous should happen than upon its truth.

THE ACT OF DYING

By HUGH BARBER, M.D., F.R.C.P.

Consulting Physician, the Derbyshire Royal Infirmary.

With what strift and pains we come into the world we remember not; but 'tis commonly found no easy matter to get out of it.—Sir Thomas Browne.

WHEN a young doctor has been in practice for a comparatively short time he will be forming well-defined views about infants entering the world, but towards the end of a long professional life he may find it no easy matter to sum up his conclusions concerning the act of leaving it. For which reason death is a subject that may appropriately claim our attention.

Familiar to most of us is Thackeray's picture of Colonel Newcome dying within sound of the old school bell, and as it tolls for evening roll-call his last word is "*Adsum*". Or in a more recent novel, "*Good-bye Mr. Chipps*", the apparently unconscious dying schoolmaster catches some remark, that it was a pity he had no children, and he exclaims with a faint chuckle: "Yes I have. Thousands of 'em—and all boys". These two simple stories seem to fit in with the spirit in which the individuals had lived. In real life the relatives would value such a remembrance. In "*Rab and His Friends*" the thoughts of the old woman, who had braved surgery before the days of anæsthesia, turned in her last hours towards the child she had lost many years previously. These are natural scenes, but there are obvious reasons why such endings are unusual.

If, for example, from history, we consider some "last words", they depend so largely upon the type of death. Nelson, about three hours after being wounded, died after saying: "Thank God I have done my duty!" Napoleon, with a mind wandering at the end of an exhausting illness, was heard to mutter something about "*tête d'armée*". And Wellington, aged eighty-three, had only time to say, "I feel very ill; send for the apothecary", before he became unconscious. In the case of Gladstone there are no recorded last words because he drifted into a state of coma lasting for a week.

Such pictures as these, from fiction or history, may be in the minds of the relatives, and to think of them may guide the doctor in his advice. We may remember the medical bulletin, over the air: "The life of His Majesty King George the Fifth is passing peacefully to its close". But the nature of the illness will not always permit of anything so clear and dignified.

Some messages suggest a certain degree of physical resignation. Samuel Johnson said "I would give one of these legs for a year more of life; I mean comfortable life, not such as I now suffer". There is Sir William Osler's remark: "I have been too far across the river to go back and have it all over again". Every doctor knows that William Hunter said: "If I had strength to hold a pen I would write how easy and pleasant a thing it is to die".

THE NATURE OF THE LAST ILLNESS

Apart from the prognosis of the natural history of the disease, a doctor

must be able to foretell something of the state of mind in the last hours. If death due to natural causes may occur soon after birth, or be postponed to the age of ninety years or more, it would be a long story to discuss every aspect, but it may be possible to consider those which chiefly concern the medical profession. In young people, in middle life or in the majority who die in hospital, there is, in the nature of the case, a struggle for recovery; hope until quite near the end; occupation with active treatment; and a fatal event likely to come without many days of warning, or with a clouded brain. The degree of consciousness towards the end varies with the disease. Drowsiness may pass to actual coma, of which a hint may have come some time previously in the form of Cheyne-Stokes' respiration. In congestive heart failure the more urgent distress may diminish as death approaches. It is characteristic of respiratory conditions that the patient suffers much less than the onlookers might suppose—unless there is obstruction high up which demands relief. Steadily progressing hypostatic congestion makes for a peaceful end.

Perhaps the most distressing deaths occur in acute abdominal conditions, when treatment has failed. There is extreme prostration, with a mind that is clear, and there is risk of vomiting or other distressing symptoms. In discussing death as an event there is the difficult decision as to when all hope of recovery should be abandoned. There is a tendency in hospital, sometimes, to carry on with treatment which is no longer beneficial. In this connexion, he is a fortunate resident who can obtain the kindly advice of a wise, experienced ward sister.

The medical aspects of sudden death, coming without warning, are few. One can only bring comfort to the bereaved by the usual statement that there has been no suffering and the distress of a lingering illness avoided. It is not possible to formulate any rules as general guidance about telling an individual, or his relatives, that there is risk of a sudden fatal seizure. Each case—to use that hackneyed phrase—must be judged on its merits. I would suggest, however, that the doctor should only have regard for these merits, which may be medical, psychological, or social, and he should not think too much about his own reputation. I remember one cautious, pessimistic doctor, who warned relatives about the possibility of sudden death in most of his elderly patients. They might have been trees in a forest with a ring round them, indicating they would be cut down. In the event, quite a number outlived the doctor.

WHAT THE DOCTOR CAN BRING TO THE RELATIVES

When there is no longer any hope of recovery, but plans have been made for nursing and relief of symptoms, there is an art in allowing the relatives to take charge, while the doctor recedes into a more secondary position. He must, however, have gained such confidence that there will be no catching at straws, or chasing false philosophies, which only lead to distress. We shall assume that it is agreed that everything possible has been done,

THE ACT OF DYING

By HUGH BARBER, M.D., F.R.C.P.

Consulting Physician, the Derbyshire Royal Infirmary.

With what strift and pains we come into the world we remember not; but 'tis commonly found no easy matter to get out of it.—Sir Thomas Browne.

WHEN a young doctor has been in practice for a comparatively short time he will be forming well-defined views about infants entering the world, but towards the end of a long professional life he may find it no easy matter to sum up his conclusions concerning the act of leaving it. For which reason death is a subject that may appropriately claim our attention.

Familiar to most of us is Thackeray's picture of Colonel Newcome dying within sound of the old school bell, and as it tolls for evening roll-call his last word is "*Adsum*". Or in a more recent novel, "*Good-bye Mr. Chipps*", the apparently unconscious dying schoolmaster catches some remark, that it was a pity he had no children, and he exclaims with a faint chuckle: "Yes I have. Thousands of 'em—and all boys". These two simple stories seem to fit in with the spirit in which the individuals had lived. In real life the relatives would value such a remembrance. In "*Rab and His Friends*" the thoughts of the old woman, who had braved surgery before the days of anæsthesia, turned in her last hours towards the child she had lost many years previously. These are natural scenes, but there are obvious reasons why such endings are unusual.

If, for example, from history, we consider some "last words", they depend so largely upon the type of death. Nelson, about three hours after being wounded, died after saying: "Thank God I have done my duty!" Napoleon, with a mind wandering at the end of an exhausting illness, was heard to mutter something about "*tête d'armée*". And Wellington, aged eighty-three, had only time to say, "I feel very ill; send for the apothecary", before he became unconscious. In the case of Gladstone there are no recorded last words because he drifted into a state of coma lasting for a week.

Such pictures as these, from fiction or history, may be in the minds of the relatives, and to think of them may guide the doctor in his advice. We may remember the medical bulletin, over the air: "The life of His Majesty King George the Fifth is passing peacefully to its close". But the nature of the illness will not always permit of anything so clear and dignified.

Some messages suggest a certain degree of physical resignation. Samuel Johnson said "I would give one of these legs for a year more of life; I mean comfortable life, not such as I now suffer". There is Sir William Osler's remark: "I have been too far across the river to go back and have it all over again". Every doctor knows that William Hunter said: "If I had strength to hold a pen I would write how easy and pleasant a thing it is to die".

THE NATURE OF THE LAST ILLNESS

Apart from the prognosis of the natural history of the disease, a doctor

tion from having our minds in sympathy with someone who has died.

DOCTOR AND PATIENT

What is the relation between the doctor and a patient who is going to die? The stage of any curative treatment is past, and so far as possible display should be avoided. Nature will take its course, and doctor and patient should be their natural selves. To a direct question from an individual as to whether recovery is possible, the best answer is something rather evasive, to the effect that there is no very special treatment, but we must rely on nature. We should encourage a condition of mental relaxation, for which endeavour it may be wise to talk of things primitive and universal, such as a childhood or school-day reminiscence, a cloud effect through the window, or some holiday picture in the room—even if it be nothing more exciting than Southend-on-Sea. He is a poor doctor who cannot find a thought suitable for the occasion.

It would be presumptuous, and scarcely a medical problem, to discuss philosophies and belief. Benjamin Franklin, when his brother died, wrote: "It is the will of God and nature that these mortal bodies be laid aside when the soul enters into real life". In contrast there is a long letter from Thomas Huxley to Charles Kingsley, examining the "mischievous and delusive" arguments for immortality. We usually deal with simpler folk than Huxley. If a strange philosophy is expounded, perhaps the doctor may find some comfort in the idea that words are only noises and have no actual meaning in themselves. Very few people really believe that they will go out like a candle; and experience teaches us that the vast majority with a clear brain make a dignified and not unhappy ending. Of course, personal circumstances have considerable influence on the state of mind. To have made some provision for dependants is a comfort. When Captain Scott and his companions died in the Antarctic, his letter of farewell, found with the bodies, made an appeal for their dependants; to which, as we know, there was a generous response. Galsworthy depicts Old Jolyon thinking about the day he got back from school just in time to find his mother dying with a clear brain. The story is true to nature, but fortunately the circumstances are rare, because a mother must feel that no one can take her place.

Sir Thomas Browne says: "Every man is not a proper Champion for Truth, nor fit to take up the Gauntlet in the cause of Verity". This is no place to dispute with Thomas Huxley about "delusive arguments" for immortality. But we can reflect about what might remain in this world. It is an idea compatible with any life worth leading, but perhaps in this respect the medical profession is favourably placed. The high lights of the profession, from Hippocrates to William Osler, have all left a spirit living in this world. Those medical men and women, who have done no more than exchange ideas and work loyally with colleagues, need not trouble about their ashes being scattered, for some of their spirit will survive. In the words of W. E. Henley: "So be my passing. My task accomplished and the long day done".

With the situation accepted that someone is in the hands of Providence or nature, it is surprising how much assistance the doctor may give; mostly in the form of reassurance. The question may be raised whether a man should be told he is going to die, although this situation may arise some little time before the expected event. Perhaps a wife has found it rather a strain to hear him talking of the future. In most cases we shall find that he has a fairly shrewd idea. He may have noticed that the more serious attempts at treatment are dropping off. He has probably picked up a hint from the doctor's words or looks. At the back of his mind, he realizes that humanly speaking his life is coming to an end; he suspects that he is just building castles in the air—and why not?—to some extent he has done it all his life. To have the admitted truth accepted by all around makes his situation uncomfortable. It is along these lines that the relatives should be advised.

They may ask about fear. More usually perhaps a son or daughter will have a dread that their father will be afraid. The practitioner may here be most reassuring, whatever his philosophy or belief. It is true that very occasionally, perhaps sometimes in an alcoholic, death is a miserable scene. Those people, however, who have let it be known through their active life—of whom Samuel Johnson is an example—that they were afraid to think about dying, have not recoiled from the event. Or the relatives may seek advice about some last message. There is the problem of being at hand. Or the use of sedatives may be criticized in this connexion. It is true that in a death from uncomplicated old age, the individual may light up for a few minutes at the finish, but it is likely to be just a simple good-bye.

The best medical advice, as a rule, is to the effect that the relatives have said good-bye in stages; they have seen the best of their patient. They should not try to call back a mind that is peacefully wandering, or discourage a sedative for an over-active brain. If there are words, the meaning of which it is not easy to comprehend, we should be content to leave them obscure—it may be just a dream. The phrase "death agony" is ill chosen. In the ordinary way dying should be peaceful, or be relieved into quietude by sedatives. Best of all there should be a good nurse. The doctor is rarely present himself. The correct attitude is to have been near at hand without intruding and to surrender his charge to the nurse in the last hours.

Occasionally the relatives will talk to the doctor, afterwards, about some form of spiritualism. This was in evidence in the 1914 war, encouraged by Sir Oliver Lodge, whose son had been killed. A few who have sought for messages have found some comfort, but to most it has only been distressing. It has seemed to me that what has purported to come at a séance or through a medium has been such trivial twaddle; it should have been clear that it was in no way related to the spirit of the life and mind of the deceased. But it is not the business of the medical profession to close the door on any honest seeking for the truth. If we reflect how, during some period of anxiety, we sometimes rather suddenly come to a decision which proves to be the right one, or if occasionally we wonder what prompted some happy idea, it is not beyond the bounds of possibility that we do get some inspira-

hardly scientific to ignore, and certainly not kindly to refuse if it can be gratified, as in the old days it usually could be.

WHEN IS A PATIENT "DYING"?

The problem which usually faces the general practitioner, i.e., that of looking after a dying person at home rather than in hospital, is in many ways a thankless job unless it is relieved by a belief in the ultimate value of personality and human kindness, and it raises many ethical and philosophical problems. It is a doctor's business to prolong life, although not necessarily to prolong the act of dying, and one question is to know where to draw the line. Looking back over thirty years' practice I can recall a number of cases in which life would almost certainly have become extinct if one had not been either near at hand or fortunate enough to hit on some remedy that stayed the hand of death, perhaps for many years. One has earned the patient's gratitude and often, at the time, that of the relatives as well. Yet how often the extra span of life has proved for the patient one of failing powers and often of deteriorating character, and for the relatives one of increasing anxiety and responsibility, so that the end is finally desired by all long before it comes. I am, of course, speaking of elderly people, except in the case of cardiovascular catastrophes which often occur in the fifties, but with a similar sequel. With younger people the outlook is much more hopeful, but it does raise the question of when is it possible to say that a person is dying? Life itself is bound to end, so that in one sense we are all dying, although we do not say so; nor should we say that a person with an incurable cancer or other disease is "dying" as soon as we know that a moderately early end is inevitable. These cases should be considered more or less as among the chronically sick, and I would say that, roughly, a patient is "dying" when ordinary remedial or palliative measures fail to have their normal effect. With heart cases, for example, there comes a time, often definitely marked, when digitalis in any dose or form no longer has any effect; when theophylline or caffeine fails to produce relief, and when the mercurial preparations produce no diuresis. From that moment it seems right to consider the care of the patient as the care of the dying. In the same way a patient with carcinoma, diabetes, asthma, or many another type of illness, will pass through a phase in which he or she can be kept fairly comfortable with certain drugs or treatment, and then, in some unknown way, the well-tried remedies fail to act, nor can substitutes be found. From then onwards they should be looked upon as dying patients.

There is a good reason for being able to distinguish the dying phase from that in which treatment can be hopeful, if merely palliative, for while there is a hope of improving the patient's condition or lot it is the duty of the medical attendant to take such steps in this direction as his skill permits. When, however, it is clear that the end is drawing near there is only one

THE CARE OF THE DYING

By W. N. LEAK, M.D.

THE care of the dying is becoming a much greater problem than it used to be. Not so many years ago the matter was relatively simple. In the days of large families there was nearly always some relative who would look after the dying person, or if there were no relatives available, handy women, more or less skilled or kindly, were much more common than they are to-day. Failing one of these, the Poor Law Institutions could usually be relied upon to take care of the process and the patient. Then too, the doctor's armanentarium was much more limited, with the result that dying now tends to be a longer procedure than it used to be, nursing standards are higher and require more apparatus and care, whilst, in contradiction to the common belief that old people are feeble folk, as a matter of fact the older a patient is the longer he or she takes to die. We are therefore reaching a paradoxical and extremely awkward situation. People are taking much longer to die than they did, partly owing to the increasing age at which death occurs (the average age in my death certificate books varies between sixty-five and seventy years), and partly because medical and nursing skill can keep them longer alive. More often than not relatives are not available or willing to undertake the care of them in their homes; the women who used to do this in the past have died, and with their old age pensions their successors see no need to turn an honest penny, and so refuse the job. Poor Law institutions have had their standards raised out of all recognition, but not the numbers of their beds or staff, so that relatively few dying people get hospital attention during their last days, except perhaps in the large towns.

So, however theoretically desirable it may seem to some that all old people should obtain the best skill and care in their dying moments, it seems pretty clear that this will remain an ideal for a long time to come. Perhaps I may question whether this really is an ideal, except from the point of view of pious relatives who may say they wish them to have the best but subconsciously really desire to avoid the trouble of looking after them. For I think it is almost undeniable that as life draws to its close, in every age and among nearly every race, there is an urge to return to the home of one's youth. When in *Ecclesiastes* 12, v, the Preacher said "man goeth unto his long home", he spoke for the whole human race, and it is one of the most pathetic things in looking after old people to notice the wistful way in which they long for home as life draws to its end. Even worse to watch is the deep distress of those who have the common delusion that although they actually are at home, they are somewhere else and that their relatives are strangers. Many animals also seem to hide away home to die, and one cannot help thinking that such a common feeling testifies to a biological urge which it is

hardly scientific to ignore, and certainly not kindly to refuse if it can be gratified, as in the old days it usually could be.

WHEN IS A PATIENT "DYING"?

The problem which usually faces the general practitioner, i.e., that of looking after a dying person at home rather than in hospital, is in many ways a thankless job unless it is relieved by a belief in the ultimate value of personality and human kindness, and it raises many ethical and philosophical problems. It is a doctor's business to prolong life, although not necessarily to prolong the act of dying, and one question is to know where to draw the line. Looking back over thirty years' practice I can recall a number of cases in which life would almost certainly have become extinct if one had not been either near at hand or fortunate enough to hit on some remedy that stayed the hand of death, perhaps for many years. One has earned the patient's gratitude and often, at the time, that of the relatives as well. Yet how often the extra span of life has proved for the patient one of failing powers and often of deteriorating character, and for the relatives one of increasing anxiety and responsibility, so that the end is finally desired by all long before it comes. I am, of course, speaking of elderly people, except in the case of cardiovascular catastrophes which often occur in the fifties, but with a similar sequel. With younger people the outlook is much more hopeful, but it does raise the question of when is it possible to say that a person is dying? Life itself is bound to end, so that in one sense we are all dying, although we do not say so; nor should we say that a person with an incurable cancer or other disease is "dying" as soon as we know that a moderately early end is inevitable. These cases should be considered more or less as among the chronically sick, and I would say that, roughly, a patient is "dying" when ordinary remedial or palliative measures fail to have their normal effect. With heart cases, for example, there comes a time, often definitely marked, when digitalis in any dose or form no longer has any effect; when theophylline or caffeine fails to produce relief, and when the mercurial preparations produce no diuresis. From that moment it seems right to consider the care of the patient as the care of the dying. In the same way a patient with carcinoma, diabetes, asthma, or many another type of illness, will pass through a phase in which he or she can be kept fairly comfortable with certain drugs or treatment, and then, in some unknown way, the well-tried remedies fail to act, nor can substitutes be found. From then onwards they should be looked upon as dying patients.

There is a good reason for being able to distinguish the dying phase from that in which treatment can be hopeful, if merely palliative, for while there is a hope of improving the patient's condition or lot it is the duty of the medical attendant to take such steps in this direction as his skill permits. When, however, it is clear that the end is drawing near there is only one

THE CARE OF THE DYING

By W. N. LEAK, M.D.

THE care of the dying is becoming a much greater problem than it used to be. Not so many years ago the matter was relatively simple. In the days of large families there was nearly always some relative who would look after the dying person, or if there were no relatives available, handy women, more or less skilled or kindly, were much more common than they are to-day. Failing one of these, the Poor Law Institutions could usually be relied upon to take care of the process and the patient. Then too, the doctor's armanentarium was much more limited, with the result that dying now tends to be a longer procedure than it used to be, nursing standards are higher and require more apparatus and care, whilst, in contradiction to the common belief that old people are feeble folk, as a matter of fact the older a patient is the longer he or she takes to die. We are therefore reaching a paradoxical and extremely awkward situation. People are taking much longer to die than they did, partly owing to the increasing age at which death occurs (the average age in my death certificate books varies between sixty-five and seventy years), and partly because medical and nursing skill can keep them longer alive. More often than not relatives are not available or willing to undertake the care of them in their homes; the women who used to do this in the past have died, and with their old age pensions their successors see no need to turn an honest penny, and so refuse the job. Poor Law institutions have had their standards raised out of all recognition, but not the numbers of their beds or staff, so that relatively few dying people get hospital attention during their last days, except perhaps in the large towns.

So, however theoretically desirable it may seem to some that all old people should obtain the best skill and care in their dying moments, it seems pretty clear that this will remain an ideal for a long time to come. Perhaps I may question whether this really is an ideal, except from the point of view of pious relatives who may say they wish them to have the best but sub-consciously really desire to avoid the trouble of looking after them. For I think it is almost undeniable that as life draws to its close, in every age and among nearly every race, there is an urge to return to the home of one's youth. When in *Ecclesiastes* 12, v, the Preacher said "man goeth unto his long home", he spoke for the whole human race, and it is one of the most pathetic things in looking after old people to notice the wistful way in which they long for home as life draws to its end. Even worse to watch is the deep distress of those who have the common delusion that although they actually are at home, they are somewhere else and that their relatives are strangers. Many animals also seem to hide away home to die, and one cannot help thinking that such a common feeling testifies to a biological urge which it is

reward—the culmination often of a long battle with death that patient and doctor have fought together with courage and determination; the acknowledgment that although the last enemy has won the patient has still confidence in his physician and that the human spirit can triumph even in the hour of defeat. It is strange how often a patient who has been practically unconscious for days will still respond in some degree when he hears the doctor's voice or feels his hand upon his pulse. It is pathetic—and exacting—how eagerly dying people look forward to the visit of their doctor, even though there is nothing the doctor can do to assist them medically. In the new Health Service I expect that this side of medical practice will disappear with the older generation of practitioners. It will be dismissed as sentimental tosh. Yet it is of the very essence of good general practice. Doctor and patient, whether of high degree or low, have come to know and respect one another, and when Death, the great leveller, comes, the unspoken trust and thanks of the crossing sweeper are just as worth winning as those of the nobility.

The question often faces the practitioner whether or not he should let the patient know that he is dying. It is almost always well to warn some relative or friend, even if only to preserve one's reputation for diagnosis and prognosis. Not infrequently there are vital family matters at stake. It is extraordinary how many people still do not make a will, and how even intelligent folk seem never to have given real thought as to what is to happen after they are gone. It is best not to let the patient actually reach the stage of dying before tackling this problem. Many will say that it is none of the doctor's business, yet innumerable families and patients have been grateful to a physician who has not taken such a narrow view of his professional responsibilities and opportunities. Not a few patients ask straight out whether they are dying. Many doctors evade the question or put it off. A great deal depends upon the patient as well as the doctor. Personally, I think that a quiet straight answer with a clear look in the eye is as a rule the best reply, and it is usually answered by a quiet "Thank you, Doctor" or "I knew it". It is vastly easier to manage the patient after such a simple and sincere acknowledgment of the fact. And if the doctor can honestly also speak of that land where "there is no more death, neither sorrow nor crying, neither shall there be any more pain" the last dying days may be full of hope and peace instead of violent struggle and despair.

NURSING

The golden rule is to give the dying as much of their own way as possible. All nursing operations should be performed as gently and as seldom as possible. A bed sore may be a disgrace to a nurse, but it is certainly less discomfort to a dying patient than frequent and painful efforts to avoid it in the last day or two of life.

Incontinence, and especially retention with overflow, are great troubles

kindly attitude to adopt, and that is to make the patient as comfortable as possible. This is, incidentally, the real secret of treating any old people; to let them have their own way, or to make them think that they are getting it. There is no surer way of rapidly finishing off an old patient than to impose on him a strict regime of any kind, whether dietary, medicinal or even just insisting on his bed being kept immaculate. In such circumstances old people rapidly come to the conclusion, consciously or otherwise, that life is no longer worth living and quickly slide away in spite of all medical and nursing care. Relax the reins as much as possible, humour them in every way legitimately possible, even if it should be against accepted canons for treating a similar state in younger patients, and it is extraordinary how often they will pick up. This is one reason why, in the larger hospitals, old people are considered bad risks. No old tree stands transplanting, and the move from the comforts, or discomforts, of a familiar home to the clean efficiency of a large hospital weighs the scales against recovery, compared with the less exacting routine of a local cottage hospital with which the patient may have been familiar for years.

Not infrequently it is the patient's friends or relatives who determine the time of the end. Most doctors will have had reason to reflect on the sinister truth of the saying "Where the carcass is, there will the vultures be gathered together", for when all sorts of lost or forgotten relatives begin to assemble about the patient's bed, eagerly looking for pickings before life is extinct, most patients sense that the end is not far off and few are deceived by the affection displayed; a feeling of hopelessness or weariness overcomes them and they give up the struggle.

I recall, however, one stout old lady who in such circumstances made a most unexpected recovery, nor could I find the reason until long afterwards when she told me that one of her daughters had come bringing a shroud and saying to her "You'll be wanting this very soon, Mother". This so infuriated the old body that she made up her mind to get better in order to cut the daughter out of her will—which she did!

THE PRACTITIONER'S RÔLE

In few departments of medicine does the treatment depend more upon the individual physician and his outlook on life in general. If he thinks that death is the end of all things and the sooner it is over the better for all concerned, then obviously a few doses of morphine or, even more rapid, no morphine at all, is all that is required. If, however, he is one who believes that kindness and goodness have absolute values and that there is some existence beyond the grave, his treatment will be much more individual and discriminating. The situation demands above all humanity and common sense. Humanity, kindness, and integrity will often be required as seldom in other branches of medicine. The gleam of recognition, the look of gratitude and trust of the dying man as he becomes aware of the doctor's presence in the room may have no financial value, but it is a most satisfying

whole it is better if feelings are not bottled up at such a time. Let them have a good weep over it and get relief that way. When one hysterical girl sets all the rest "a-sighing and a-sobbing", it is wise to put the brake on somehow, usually by giving one or two something definite to do, and by giving the ringleaders a good dose of a barbiturate with a cup of tea. I find that seconal sodium seems to do better than other preparations at such times; it acts quickly and its bright red capsule appeals to the fairer sex, added to which if the woman foolishly keeps it in her mouth it is not long before its bitter taste makes her thankful to take a good drink and swallow it properly.

MEDICAL TREATMENT

I have left to the end the purely medical treatment of the dying. It can almost be written in one word—morphine. There is no drug to touch it for dying folk, and after a preliminary testing dose there is no need to fear overdosage. Contrary to common belief morphine does not hasten the end, unless the patient is abnormally sensitive or an overdose is given. Actually it prolongs life in an amazing way, probably by its effect on slowing metabolism and so reducing the demands of the organism for oxygen; in fact, many a patient who is expected to die within twenty-four hours will, under the influence of morphine, last for a week. Morphine by itself is, however, rather capricious in its action. To quieten a rough patient, unduly large doses may have to be given, and morphine by the mouth is especially uncertain, probably due to impaired absorption; furthermore, it is much more constipating than morphine given hypodermically. It is best to give the drug alone to start with, but as soon as some idea of the patient's reaction to it is obtained it is advisable to add some hyoscine. *Hyoscine* can be unexpectedly fatal in some cardiac cases, in which it should only be used very sparingly at first, but it greatly prolongs the sedative action of morphine, enabling a much smaller dose to be used, and there is usually less excitement in the early stages and less nausea afterwards, whilst its amnesic properties are most valuable. It is unfortunate that unless a trained nurse is present the administration of morphine hypodermically means that the doctor has to attend morning and evening to give it himself. Whether or not it is worth his while to do so, each doctor must decide for himself, but there can be no doubt of the comfort it affords to the patient and his family. *Pethidine* can, of course, be used instead of morphine if the latter's sedative action is not required, or if it is desired to keep the brain particularly clear for some legal or family reason. The use of oxygen is not indicated for dying folk unless there is some desperate need to prolong life for some relative to arrive or a will to be signed. The sedative action of the barbiturates is more than usually uncertain in dying people, although they may sometimes be used with benefit when it is impracticable to give a hypodermic injection of morphine.

with old dying folk. A distended bladder will keep a patient restless, whether he has a fractured base or has received a large dose of morphine. To overlook this is one of the most common faults in nursing the dying. In such cases there is no need to go through the slower emptying of the bladder that would be employed in younger or more hopeful patients. If, as sometimes happens, after his bladder has been emptied the patient falls into a restful slumber from which he never awakens it is a merciful ending for which everyone should be thankful, whatever the pathology may be. More often the bladder fills up again, and if it is emptied morning and evening by catheter it makes the work of nursing very much lighter. A urine bottle may sometimes catch quite a lot of urine in cases of true incontinence if the patient is very quiet, but more often than not the best thing seems to be to truss him up like a baby in a napkin and change these several times a day.

The bowels are often a great nuisance, although with old people it is amazing how seldom the abdomen gets blown up with wind during the dying period. If they are opened every three days it is ample, and if the patient is lying comatose it does not matter if the period is still longer. In most cases it is best to avoid giving laxatives to dying folk. They are not only uncertain in their action but in the time of action, with the result that dirty beds and needless discomfort and washing are occasioned. The most simple thing to do is to insert a glycerin suppository, and in a large number of cases this will do all that is necessary. Failing this an enema every three days is the best, but the trouble with enemas in dying people is that often the sphincter is weak or relaxed and the enema contents run out again without doing any good. Often scybalous masses lie just inside the rectum and require digital removal. This is an unpleasant business for attendant and patient, but I know of no other method of relieving the trouble, and the removal of such a hard mass will often give great relief to the patient.

The care of the mouth is an important item in nursing, and patients are usually glad to have their mouths cleaned out with some refreshing type of mouth wash, and so long as the patient likes it, it does not matter much which kind of mouth wash is used. When the patient is comatose there is not much point in keeping the lips moist. If the relatives or friends wish to do this there is certainly no harm in it, and it is often useful in keeping them quiet by giving them something to do.

THE RELATIVES

By this stage, management of the relatives and friends has become more important than the management of the patient, and here also the doctor finds plenty of scope for the exercise of his humanity and common sense. What he can do depends very largely upon how intimately he knows the family. Is it advisable to be strictly and even coldly professional? It may help to damp down some of the more hysterical people present, but on the

whole it is better if feelings are not bottled up at such a time. Let them have a good weep over it and get relief that way. When one hysterical girl sets all the rest "a-sighing and a-sobbing", it is wise to put the brake on somehow, usually by giving one or two something definite to do, and by giving the ringleaders a good dose of a barbiturate with a cup of tea. I find that seconal sodium seems to do better than other preparations at such times; it acts quickly and its bright red capsule appeals to the fairer sex, added to which if the woman foolishly keeps it in her mouth it is not long before its bitter taste makes her thankful to take a good drink and swallow it properly.

MEDICAL TREATMENT

I have left to the end the purely medical treatment of the dying. It can almost be written in one word—morphine. There is no drug to touch it for dying folk, and after a preliminary testing dose there is no need to fear overdosage. Contrary to common belief morphine does not hasten the end, unless the patient is abnormally sensitive or an overdose is given. Actually it prolongs life in an amazing way, probably by its effect on slowing metabolism and so reducing the demands of the organism for oxygen; in fact, many a patient who is expected to die within twenty-four hours will, under the influence of morphine, last for a week. Morphine by itself is, however, rather capricious in its action. To quieten a rough patient, unduly large doses may have to be given, and morphine by the mouth is especially uncertain, probably due to impaired absorption; furthermore, it is much more constipating than morphine given hypodermically. It is best to give the drug alone to start with, but as soon as some idea of the patient's reaction to it is obtained it is advisable to add some hyoscine. *Hyoscine* can be unexpectedly fatal in some cardiac cases, in which it should only be used very sparingly at first, but it greatly prolongs the sedative action of morphine, enabling a much smaller dose to be used, and there is usually less excitement in the early stages and less nausea afterwards, whilst its amnesic properties are most valuable. It is unfortunate that unless a trained nurse is present the administration of morphine hypodermically means that the doctor has to attend morning and evening to give it himself. Whether or not it is worth his while to do so, each doctor must decide for himself, but there can be no doubt of the comfort it affords to the patient and his family. *Pethidine* can, of course, be used instead of morphine if the latter's sedative action is not required, or if it is desired to keep the brain particularly clear for some legal or family reason. The use of oxygen is not indicated for dying folk unless there is some desperate need to prolong life for some relative to arrive or a will to be signed. The sedative action of the barbiturates is more than usually uncertain in dying people, although they may sometimes be used with benefit when it is impracticable to give a hypodermic injection of morphine.

THE YOUNGER PATIENT

Younger people show such powers of recovery that they should never be considered to be dying until they are dead, unless suffering from some chronic pulmonary, cardiac, renal or malignant disease. Every effort should be made to prevent the onset of death until it has actually happened. It is perhaps presumptuous of a general practitioner to suggest remedies which are not in universal use, but as the basis of science is observation and not authority I add a few words on some measures I have used with success for many years, as they are well within the scope of any general practitioner, even if neglected by the more learned.

I suppose that the most common cause of death after abdominal operations in our smaller hospitals is *paralytic ileus*. There are all sorts of ways of dealing with this, but it seems strange that the old-fashioned method of giving intravenous pituitrin is so seldom employed. Its action is often so rapid that it is wise to have the patient actually sitting on a bed-pan, as flatus and fæces are frequently passed before the slow injection of 1 c.cm. is completed. Its main objection is the unpleasant though transient shock that often accompanies the procedure, but recently I have found that the injection of 1 c.cm. of cardiazol-ephedrine about five minutes beforehand reduces this risk considerably.

Another bugbear of surgical practice is *death or collapse under an anæsthetic*. It still seems common practice to trust to coramine to treat this emergency, whereas in actual fact it cannot compare in effectiveness with cardiazol-ephedrine, which acts in a way that would scarcely be credited by those who have not witnessed it. I am thankful to say that I have had no experience of actual deaths under an anæsthetic, but from my experience with babies I feel fairly sure that an intraventricular injection of 2 c.cm. of cardiazol-ephedrine is at least as likely to resuscitate the patient as the more dramatic and difficult cardiac massage. I have previously described this procedure for apparently still-born babies, and I have used it seven times with success in the past seven years. The last case is worth quoting as it is unique in my experience.

Ten weeks ago a twenty-five year old primipara with Still's disease and a rather small pelvis had a not very difficult forceps delivery. The baby breathed quite normally, but about twenty minutes later became blue and in a few minutes had passed into typical white asphyxia. Subcutaneous cardiazol-ephedrine produced no effect, but 0.5 c.cm. injected into the left ventricle started breathing and crying within a minute, and, to my surprise, the baby has remained healthy ever since.

With penicillin and the sulphonamides one would think that most acute infections should be overcome, but sometimes they seem to be started too late and one feels that if the patient had only lived a while longer the result would have been different. Treatment of the moribund patient with intragluteal injections of dekadexolin (a concentrate of vitamins A and D first made for me by Glaxo Laboratories nineteen years ago) can be relied upon

to give that extra twenty-four to forty-eight hours of life in cases of serious infection, and it improves the general condition of the patient in a way which is not possible in general practice outside the resources of a large hospital. I do not know how it acts, but of its effectiveness I have no doubt, especially in desperate cases.

Sedatives.—Many patients die because they are simply worn out, and from the experience of my patients in large modern hospitals I am surprised how relatively seldom sedatives are used. Proper rest is a life-saving measure in many patients, especially in children. Soneryl (or sonalgin) has, in my hands, proved the most generally useful for small children or even infants, although for infants phenacetin and caffeine (1 grain [65 mgm.] of phenacetin and $\frac{1}{4}$ grain [16 mgm.] of caffeine for each year of age up to four, given every four hours) have an uncannily satisfactory sedative effect, especially if there is any fever or pain, and the dose given can sometimes be exceeded with advantage. When, however, drugs by mouth are impossible or undesirable I have found nothing so satisfactory for children as small doses of somnifaine intramuscularly. It can be repeated indefinitely as often as required. It is somewhat slow-acting, so that there is plenty of warning of when another dose is necessary, and I am sure that many of my small patients owe their lives to its use, by conserving their strength yet not preventing their feeding or other bodily functions.

CONCLUSION

Much more might be said on most of these topics, but, as is probably too obvious, what has been written has not been culled from books but is the result of experience, often gained by fumbling with no one more experienced at hand to guide me, but all the time building on the great tradition of medicine that, come what may, the patient's interest comes first, and that the physician has a duty to his patient that is not discharged until the last breath has been taken and the flickering pulse is still.

SOME MEDICAL AND LEGAL PROBLEMS OF DEATH

By SYDNEY SMITH, C.B.E., M.D., F.R.C.P.

Regius Professor of Forensic Medicine, University of Edinburgh.

It is often said that the practising doctor has little or no concern with the dead body or with the subject of death itself; and it is certainly true that his professional interests need not involve him in the metaphysical considerations with which the subject is so commonly associated. But he can hardly fail to realize that much of his special knowledge has been derived from a study of the dead body, and that even to-day, in an era of biochemistry and "vital" pathology, the cadaver remains an important field of investigation and a fruitful source of information. Every death provides food for reflection on those fundamental morbid processes which are so much more important than the mere name of a disease, and in considering the causation of death we are inevitably reminded of the requirements of life itself, and of the essential unity of the individual as a whole.

HAS DEATH OCCURRED?

Apart from such general considerations, however, the fact of death may confront the practitioner with a number of immediate practical problems. The young doctor, called for the first time to see a dead body, may be in real doubt as to whether death has actually occurred. The body will still be warm, the features may be strikingly "life-like", and there will probably be no external evidence to help him in making his decision. When death is due to a short period of immersion in water, or to the passage of an electric current, his uncertainty will often be shared even by his more experienced colleagues. Even when the death of an individual, as such, can be ascribed to a particular moment in time, the death of the body also implies a gradual failure in cellular vitality throughout that body; a process lasting several hours. In certain circumstances, and in the earliest stages, this process is not necessarily irreversible. These are the cases of apparent death from drowning or electrical shock, or under anæsthesia, in which resuscitation methods prove successful, and the victim is "revived". Similar methods would obviously be out of place and unavailing when the process of death had been initiated and the cells of the body already devitalized by the effects of established disease.

Tests.—There are many tests for the presence of death, all of some value. But the method of choice for the medical practitioner is obviously auscultation with the stethoscope—over the apex for sounds, however feeble, of circulatory activity; over the trachea or bronchi for sounds of respiration. The sounds may be widely spaced, and therefore auscultation should be

continuous for five minutes; or they may be very feeble and atypical, and therefore there should be absolute silence in the vicinity. Cessation of circulation and respiration throughout five minutes' continuous auscultation is satisfactory proof of death, but, of course, when hope exists, the critical five minutes cannot be occupied in this manner, and resuscitative measures should be started expectantly. When they are likely to be crowned with success, a degree of improvement in the circulation and respiration will probably be discernible within fifteen minutes, again by careful auscultation, but without the same strict necessity for silence and continuity. In the unlikely event of doubt persisting as to the fact of death, it can be resolved with certainty by delaying for a few hours, when the development of undoubted post-mortem phenomena will settle the issue.

POST-MORTEM CHANGES

The practitioner should bear in mind the nature and significance of these post-mortem changes. The dying down and cessation of metabolic activity mean the cessation of heat production, and the dead body, like any other inanimate object, loses its heat by radiation, convection and conduction. The cooling of the body is progressive, but not evenly so. Heat loss is most rapid during the first six hours or so after death, when the difference between the temperature of the body and of the environmental atmosphere is greatest, and the surface of the body, except in the flexures, feels quite cold to the touch in about ten hours. As the difference in temperature becomes minimal, the rate of heat loss becomes very slow, and it is exceptional to find the internal body warmth completely lost in less than about thirty hours. Often the time is much greater; but there is considerable variation according to the season of the year, the situation of the body, its coverings and its state of nutrition.

The development of *rigor mortis* is another post-mortem phenomenon of unusual interest. During the first ten or twelve hours after death, the original limp, flaccid state of the muscles throughout the body is replaced by a firm, "solid", partially contracted condition which often gives the body an unnaturally athletic appearance, and a board-like stiffness which can be broken at the joints only by the exercise of considerable force. The change appears first in four or five hours in the muscles about the face and neck, and spreads downwards over shoulders, trunk and limbs until the whole body is affected. After persisting for a day or two it passes off, usually in approximately the same order as that in which it developed. The development of *rigor mortis* is hastened by a high environmental temperature and by any pre-existing degree of muscular exhaustion. The more rapidly it develops, the shorter is its duration.

The chemical changes which accompany, and are responsible for, *rigor mortis* resemble to some extent those of muscular activity. There is a diminution in glycogen and an increasing acidity of the muscles. The similarity is only partial, however, and the recent work of Szent-Györgyi indicates that the essential factor may well be the gradual diminution in the adenosine triphosphate content of the muscle, which

sets in after death and is probably responsible for the physical change in the muscle proteins from a "sol" to an irreversibly contracted "gel" condition. The disappearance of rigor mortis is due to the breaking down of the muscle proteins altogether.

About the time that rigor mortis is passing off, the first external evidence appears of those *putrefactive changes* which result eventually in the complete liquefaction and dissolution of the body. Putrefaction is due essentially to bacterial activity, and the earliest changes are usually due to the bacteria which form the natural flora of the alimentary and upper respiratory tracts. Subsequently, the changes are hastened by the advent of air-borne bacteria, and a great variety of organisms—aerobes, facultative anaerobes, and anaerobes—share in the ultimate disintegration of the body. Therefore the factors which modify the rate of putrefaction are obviously those which tend to favour or inhibit bacterial activity—temperature, moisture, access of air, and the state of the body before death. In general, it can be said that the body putrefies twice as fast in air as it does in water. The rate of putrefaction in a buried body depends very much upon the conditions of burial and the nature of the soil. Exceptionally (in this country), the body may become dried up and mummified instead of undergoing putrefaction, and in water or very wet earth the putrefactive processes may be halted and modified by the occurrence of adipocere formation.

PHENOMENA OF MEDICO-LEGAL SIGNIFICANCE

These post-mortem changes are of the greatest practical value in estimating the time that has elapsed since death, usually in connexion with cases of medico-legal importance. It is becoming increasingly uncommon for general practitioners to carry out the entire investigation of such cases, including the post-mortem examination, but it is usually a practitioner who is first called to the scene, and who therefore makes the initial medical inspection of the body. The value of his observations may well be critical, and he should invariably note the state of rigor present, and also whether or not any warmth is discernible by the examining hand applied to the surface of the body and in the flexures. He may not wish to disturb the body, but these observations can be made without doing so. On occasion, he may be able to take the rectal temperature also, although, of course, a clinical thermometer is not adapted for this purpose and there may not be available to him an ordinary thermometer such as is required. The earlier the observations are made, the more accurate is the possible estimate. Within the first twenty-four to thirty-six hours it is often possible to estimate the time since death within very narrow limits indeed. Later on, when putrefaction has progressed to any considerable extent, the estimate becomes much more general. It is, of course, impossible to draw up a strict timetable—there are too many modifying circumstances. All possible data must be collected and the influence assessed of those factors which apply in the case under consideration.

Occasionally, the post-mortem change described as *hypostatic discoloration*—due to the gravitation of fluid blood into the dependent parts and its

clotting there—may be of value, not only in estimating the time since death and in deciding whether the body has been moved after death, but also in suggesting the cause of death. Normally, the discoloured areas are of a dusky, purplish-blue colour, but in carbon monoxide poisoning they have a distinctly pink appearance. In other conditions, e.g. poisoning by prussic acid or potassium chlorate, the colour may be cherry-red or chocolate brown, respectively. In acute asphyxial deaths, the blood tends to remain fluid for an unusually long period, and the hypostatic discoloration will be extensive and very dark. Isolated patches of hypostasis may be mistaken for bruises, but their distribution, uniform colour, and the absence of associated swelling or abrasion will usually serve to differentiate the two conditions. Above all, if the area is cut into, the blood will be seen to emerge from the cut ends of dilated vessels, whereas in bruises the blood is extravasated through the tissues of the part.

Injuries and blood stains.—When true bruising, or any other type of injury, is present on a dead body, the medical examiner should be particularly accurate and detailed in his descriptions. The legal authorities expect, and have a right to expect, that doctors are trained in observation, particularly of such matters as affect the human body. A note should therefore be made of the precise position and measurements, the nature, direction and extent of all injuries, no matter how trivial. Particular importance naturally attaches to such wounds as may have been the actual cause of death, but even trivial abrasions may be of significance in the reconstruction of events. The relationship of wounds to blood stains present and the character and distribution of the blood stains themselves are additional matters which should receive the doctor's attention. It is of great importance that notes should be made, fully and accurately, in all cases of violent or suspicious death, and that they should be made at the first opportunity, for there is not likely to be a second.

CERTIFICATION OF DEATH

The great majority of deaths in ordinary practice, however, are due to natural causes, and the doctor has been in attendance on the deceased during his last illness. When this is so, and the doctor is satisfied that he knows the cause of death, he is required to furnish for the Registrar a certificate of death. This will generally occasion little or no difficulty, but the doctor should invariably see the body before issuing the certificate. Occasionally, the statement of the precise nature and sequence of the causal factors may require some consideration. A little time and thought over the completion of a death certificate is well spent, because it is a document of considerable legal and statistical importance.

In other circumstances, usually when the death is sudden and the deceased is either unknown to the doctor or has not been seen by him for some considerable time, the doctor is not in a position to state the cause of

death with any certainty, and he should not attempt to do so. It is not sufficient to rely upon the statements of relatives or others, or even upon his own inferences, drawn perhaps from the age, sex, physical habit of the deceased, and so on. It is a mistaken kindness, and indeed an act of weakness, to issue a certificate in these circumstances, because occasionally the doctor who does so will be compounding a felony, and in any event the shortcomings of the certificate will be noted by the Registrar, and so brought to the notice of the Coroner. Therefore although there is no legal obligation laid upon the practitioner to inform the coroner of *any* death, his correct course in dubious circumstances is to refrain from issuing a death certificate, and to communicate directly with the coroner or his officer, or with the police, whichever appears to be the more appropriate and convenient. In Scotland there is no coroner, and the appropriate legal authority for corresponding purposes is the Procurator Fiscal for the district.

Once the matter has been reported to the coroner, no post-mortem examination or other interference with the body is permissible except on the express written instructions of the coroner. In Scotland, the procurator fiscal issues instructions for any such examination, on the authority of a warrant from the Sheriff to do so. It is not illegal for a doctor to perform a post-mortem examination before the coroner is informed, even in cases of violent, unnatural or suspicious death, provided he has the consent of the appropriate relative, but it is highly undesirable that he should do so. In other cases, however, it may only be at post-mortem examination that the unnatural nature of the death is ascertained or verified; the doctor should then inform the coroner immediately and his death certificate should be made out in accordance with his findings at the autopsy.

LEGAL POSSESSION AND DISPOSAL

The law does not recognize a dead body as constituting "property", but it does recognize that the personal representatives of the deceased have an interest in, and indeed a responsibility for, the proper disposal of the corpse—failure to do so constitutes a misdemeanour. It follows that these representatives must be considered as having certain rights in connexion with the body and, although these are not precisely defined in law, they include the right to give or withhold consent to a post-mortem examination. It may be that, in certain circumstances, a post-mortem examination carried out without consent would not necessarily be *criminally* illegal, but the relatives would be able to raise a civil action for damages. If permission is refused and the cause of death is unknown or uncertain, the doctor should refrain from issuing a death certificate, notify the coroner, and await his instructions.

Cremation as a means of disposal has much to recommend it, but because of the completeness of the destruction, it is obvious that the method must be subject to supervision lest it facilitate disposal of bodies without adequate investigation in cases of unnatural death. Application for crema-

tion is made by the executor of the deceased, or the nearest relative or other party responsible for the disposal of the body, on a form (Form A) which provides for a statement of various relevant particulars. The application concludes with a solemn declaration that the contained statements are true, which must be made before a Justice of the Peace or a Commissioner for Oaths. This application must be supported by two medical certificates. The first of these (Form B) is completed by the doctor who has attended the deceased before his death and who has seen the body after death. The particulars required by this certificate are designed to reveal whether there was anything in the deceased's illness or mode of death which might suggest unnatural causes—in particular, violence, poison, privation or neglect. The second, or confirmatory medical certificate (Form C), must be completed by a practitioner of not less than five years' standing who is neither a relative of the deceased nor a relative or partner of the first certifying doctor. The certificate requires him to indicate the nature of his inquiries in the case, and that he is satisfied as to the cause of death. In the usual case, these three documents are submitted to a specially appointed Medical Referee, who, if satisfied, authorizes the cremation (Form F). If he considers it advisable, the medical referee may first require a post-mortem examination, and if the results of such an examination are satisfactory, they are so certified by the pathologist (Form D). When the case has been in the hands of the coroner, a coroner's certificate (Form E) is required, showing the results of his inquiry and stating that no further examination of the body is necessary. By these safeguards it is ensured that there shall be no improper or ill-advised disposal of a dead body by the irrevocable process of cremation; but, of course, for their proper efficacy it is essential that they should never be allowed to degenerate into mere formalities. The completion of any cremation form is a responsible act and should be regarded as such.

As already indicated, the executor or nearest relative of the deceased has a right to the possession of the body and a right to decide on the method of disposal. In the absence of executor or relative, similar rights and responsibilities may devolve on other parties. It follows therefore that previously expressed wishes on the subject of disposal by the deceased are not legally binding. Under the Anatomy Act, 1832, it is laid down that a person may legally direct that his body be handed over for anatomical dissection after death, but even this direction may be overruled if the deceased person's nearest surviving relatives shall require the body to be disposed of without such examination. The relative's rights include the right to choose disposal by cremation, but a special provision is made by the Cremation Act, 1902, and the Rules and Orders made thereunder, that a dead body shall not be cremated when the deceased is known to have left a written direction to the contrary. The rules also provide that it shall not be lawful to cremate any body in any place other than a crematorium approved for the purpose by the Secretary of State, or to cremate a body which has not been identified.

EMBALMING AND CREMATING

By G. S. LEAR

Member of the British Institute of Embalmers.

WHEN a natural death occurs in the home, the attending physician is required to issue a certificate of death to the appropriate Registrar for the purposes of registration. Occasionally he may advise immediate removal of the body, or he may advise the quick disposal, but rarely are the bereaved advised regarding the laying-out, and in advising urgent removal or burial no consideration is given to those who have to arrange the practical details. It must be obvious that before a body is removed from a house there must be somewhere to deposit it, and before it can be buried a coffin must be made, a grave dug, and a clergyman chosen. This all takes time and is the work of the specialized funeral director.

THE LAYING-OUT

The first duty must obviously be the laying-out or, to use the hospital expression, "last offices". This usually comprises straightening, washing and dressing the body, plugging the orifices, setting the lower jaw and closing the eyes, and changing the bed linen. This work is done by the nurse in attendance or by relatives, or by a person who is known in the district to be on call. Obviously also, the work should be done as soon as possible following death, preferably before the onset of rigor mortis, although it is possible to do this work afterwards. It is not at all infrequent to find a dish of salt placed on the abdomen, presumably to prevent subsequent distension, but the actual origin or reason for this practice is obscure.

The flexed extremities should always be straightened before the onset of rigor mortis and here again it is usually regarded as the work of the nurse, although the manual strength required would indicate that it is better to have the services of the funeral director or embalmer. More difficult cases are those in which the legs or arms have contracted towards the trunk owing to rheumatoid arthritis or the like. These are usually left in the contracted position for the funeral director to correct as best he can when the body is placed in the coffin. More precise details will be given later on in this article. It is usually at this point that the funeral director takes over the case and the subsequent work depends entirely upon his ability and enterprise.

EMBALMING

It is of interest to note that a fair estimate of cases prepared for burial by the process of embalming has increased from almost zero to approximately one-fifth of the death rate in the past fifteen years, and it is reasonable to assume that if this present rate of increase continues, we may expect pre-

burial sanitary treatment of the dead to reach saturation point in the course of the next decade or so.

The process of embalming is, in broad terms, merely the complete irrigation of the vascular system by a disinfecting solution injected into one or more of the main arteries, the blood being simultaneously drained from one or more of the main veins. The operation is usually completed from one point, this being either the axillary, femoral or carotid artery, the choice of vessel being decided by the conditions prevailing and the diagnosis. The chemical employed is basically a solution of formalin, glycerin and borax, with modifications according to individual preference and the addition of colouring matter to restore the natural complexion to the tissues. The strength of the solution is adjusted to procure a satisfactory reaction according to the state of the tissues. The satisfactory distribution of the embalming chemical, injected at a pressure of approximately 1 to 1.5 lb. per square inch, removes all traces of cyanosis and hypostasis, and the massage of the exposed parts during the course of the injection results in the natural contours also being completely restored.

Following upon the arterial injection and venous drainage, the normal or abnormal body fluids are aspirated by means of special negative pressure apparatus and the use of a long trocar, and parts and substances not receiving a supply of embalming chemical in the course of the arterial injection, i.e., the faecal matter in the alimentary tract and/or any specified or diagnosed diseased areas, are cared for by a direct injection of concentrated embalming chemical.

It will be obvious that it is advisable for the operator to have a detailed clinical knowledge of the case upon which he is working, and for this work to be carried out with the least possible delay following death, as the post-mortem changes in the blood give rise to quite unnecessary circulation difficulties, and the breaking down of the lung tissue gives rise to loss of embalming chemical *via* the respiratory vessels.

Following some *autopsies*, difficulties arise in obtaining a satisfactory circulation through the facial arteries, as in the removal of the trachea and tongue it often happens that not only are the carotid arteries completely severed, but much unnecessary mutilation is done by careless dissection. This results in the external carotid and its branches being difficult to locate and inject, but it must be stated that whenever this matter has been mentioned to the pathologist the fullest cooperation has been secured.

Difficulty is sometimes experienced in hiding the incisions in autopsy cases, especially when the medial incision is taken to a point immediately below each ear. The more usual method is to stop near the thyroid cartilage. Care should also be taken to ensure that the cranial incision is made well back and its extremities kept behind the ears. As in these cases the trunk has to be opened and emptied again for the location and injection of the subclavian and iliac vessels and the thorough cleansing and disinfection of the viscera, the common and most satisfactory procedure is for the embalmer to follow immediately after the examination, while the body is still left open.

SPECIAL TREATMENT IN EMBALMING

It is of no concern in this article, or to the practising embalmer for that

matter, to inquire into the causes of disease. It is sufficient to know whether or not the disease is transmittable and the specific treatment for the case. Brief mention of the peculiarities of certain conditions will give the reader sufficient idea of how each and every type of organic disease requires its own special consideration.

Anasarca.—Here, of course, there is an accumulation of fluid in the intercellular spaces, and saturating the tissues. The necessary treatment demands that the dropsical fluid and any impurities it may contain be replaced with preservative solution. To this end the embalmer employs in the first stages of the injection a solution containing not more than $1\frac{1}{4}$ per cent. of absolute formaldehyde, so that the endothelial membrane of the capillaries may not become seared and so prevent the osmosis of this fluid into the lymph spaces. The action of injecting too strong a solution is dangerous, in so far as a formaldehyde content of over $1\frac{1}{4}$ per cent. would quickly coagulate the albumin even should it pass the capillary wall, and thus prevent the proper dissemination of the chemical and the removal of the dropsical fluid. It will be understood, of course, that the relationship between the lympho-vascular system and the venous system permits the thorough drainage of this excess moisture, provided the conditions existing are taken into consideration and the flow of the dropsical fluid is assisted either by elevation or massage, or both. Once the capillaries have been "toughened up" to resist a stronger solution, the percentage of absolute formaldehyde is increased by progressive steps to a maximum of approximately $2\frac{1}{2}$ per cent. absolute.

Edema.—The treatment of an œdematous condition depends largely upon its location, and generally the area is treated in much the same way as in anasarca. Should the œdema be consequent upon a cancerous condition, it is necessary to locate the extent of the causative disease. Immediately after injection, the excess lymph is expressed by way of incisions made posteriorly, and by means of rubber bandages wound tightly from the distal portion of the part to the proximal.

Atheroma.—Much depends upon the extent and development of the condition. It may, for instance, affect one or more arteries supplying a part where the collateral circulation was not sufficient to convey the embalming fluid. In such a case, depending upon the location, it may be necessary to continue the injection beyond the point of the blockage, but if this proves impossible, then the operator has to resort to hypodermic injection of the part not receiving the chemical arterially—a most tedious and difficult process.

Aneurysm.—Here the operator may have to make what is known as a 12-point injection, for should the aneurysm be situated in the trunk it would be possible to locate it without deep dissection, which the conscientious embalmer, with a view to potential subsequent inquiry, employs every means to avoid. The 12-point injection includes the raising and

injecting in both directions of the right and left carotid, the right and left axillary, and the right and left femoral arteries.

Reverting now to the *transmittable diseases*, the embalmer is immediately confronted with a different problem. Here there is danger not only of the cadaver not looking its best for presentation to the relatives but also the necessity of making such a case perfectly safe for those who are to come in close contact. Whenever the embalmer knowingly confronts pathogenic bacteria he takes still greater precautions in his technique—thoroughly washing the entire surface of the body and completely irrigating any localized areas of infection.

Pulmonary tuberculosis.—In this disease the causative bacteria are highly resistant to disinfectants. Often there is rapid decomposition, with oral and nasal discharges. Owing to the tenseness of the connective tissues, the abdominal wall, under the gaseous pressure resulting from decomposition, cannot distend to the same degree as it can in normal cases; it therefore takes the line of least resistance. This means that the pressure is consequently exerted against the diaphragm and thorax and, as the lung tissue is usually broken down, the blood is forced from the capillaries into the alveoli and so through the bronchioles, bronchi and trachea to discharge through the nose and mouth. As this discharge contains varying quantities of tubercle bacilli the utmost care is required on the part of the embalmer.

In cases of *deformity* and *rheumatoid arthritis*, it is necessary at least to straighten the legs, although this cannot be accomplished by normal methods. The procedure is to incise the tendons forming the boundary of the popliteal fossa and secure a splint in position. This should never be done until after the embalming treatment, otherwise the loss of embalming fluid seeping from the severed tissues would interfere considerably with the operation.

The advantages of this hygienic treatment are apparent to the professional mind, but to the bereaved the psychological effect of a properly embalmed cadaver is very great indeed. The embalmer is concerned with the appearance equally as much as with sterilization, and it will be realized that the closing of the eyes and mouth, hair dressing, shaving (if a male), positioning, dressing and make-up of the body are points which are embraced in the treatment and make all the difference to the finished results. This technique also means that the deceased can be left as though peacefully sleeping in bed until the actual time of the funeral, thereby avoiding all the gruesome accoutrements of the death chamber.

Items ancillary to the expeditious treatment of the dead body, which is the embalmer's chief concern, are the early clearance by the attending physician and/or coroner in the case of subsequent inquiry, and/or the issuing of the disposal certificate by the Registrar concerned. Not infrequently a person dying on a Friday cannot be cleared as regards the Registrar until some time on the following Monday or Tuesday. In this lapse of time,

matter, to inquire into the causes of disease. It is sufficient to know whether or not the disease is transmittable and the specific treatment for the case. Brief mention of the peculiarities of certain conditions will give the reader sufficient idea of how each and every type of organic disease requires its own special consideration.

Anasarca.—Here, of course, there is an accumulation of fluid in the intercellular spaces, and saturating the tissues. The necessary treatment demands that the dropsical fluid and any impurities it may contain be replaced with preservative solution. To this end the embalmer employs in the first stages of the injection a solution containing not more than $1\frac{1}{4}$ per cent. of absolute formaldehyde, so that the endothelial membrane of the capillaries may not become seared and so prevent the osmosis of this fluid into the lymph spaces. The action of injecting too strong a solution is dangerous, in so far as a formaldehyde content of over $1\frac{1}{4}$ per cent. would quickly coagulate the albumin even should it pass the capillary wall, and thus prevent the proper dissemination of the chemical and the removal of the dropsical fluid. It will be understood, of course, that the relationship between the lympho-vascular system and the venous system permits the thorough drainage of this excess moisture, provided the conditions existing are taken into consideration and the flow of the dropsical fluid is assisted either by elevation or massage, or both. Once the capillaries have been "toughened up" to resist a stronger solution, the percentage of absolute formaldehyde is increased by progressive steps to a maximum of approximately $2\frac{1}{2}$ per cent. absolute.

Edema.—The treatment of an œdematous condition depends largely upon its location, and generally the area is treated in much the same way as in anasarca. Should the œdema be consequent upon a cancerous condition, it is necessary to locate the extent of the causative disease. Immediately after injection, the excess lymph is expressed by way of incisions made posteriorly, and by means of rubber bandages wound tightly from the distal portion of the part to the proximal.

Atheroma.—Much depends upon the extent and development of the condition. It may, for instance, affect one or more arteries supplying a part where the collateral circulation was not sufficient to convey the embalming fluid. In such a case, depending upon the location, it may be necessary to continue the injection beyond the point of the blockage, but if this proves impossible, then the operator has to resort to hypodermic injection of the part not receiving the chemical arterially—a most tedious and difficult process.

Aneurysm.—Here the operator may have to make what is known as a 12-point injection, for should the aneurysm be situated in the trunk it would be possible to locate it without deep dissection, which the conscientious embalmer, with a view to potential subsequent inquiry, employs every means to avoid. The 12-point injection includes the raising and

injecting in both directions of the right and left carotid, the right and left axillary, and the right and left femoral arteries.

Reverting now to the *transmittable diseases*, the embalmer is immediately confronted with a different problem. Here there is danger not only of the cadaver not looking its best for presentation to the relatives but also the necessity of making such a case perfectly safe for those who are to come in close contact. Whenever the embalmer knowingly confronts pathogenic bacteria he takes still greater precautions in his technique—thoroughly washing the entire surface of the body and completely irrigating any localized areas of infection.

Pulmonary tuberculosis.—In this disease the causative bacteria are highly resistant to disinfectants. Often there is rapid decomposition, with oral and nasal discharges. Owing to the tenseness of the connective tissues, the abdominal wall, under the gaseous pressure resulting from decomposition, cannot distend to the same degree as it can in normal cases; it therefore takes the line of least resistance. This means that the pressure is consequently exerted against the diaphragm and thorax and, as the lung tissue is usually broken down, the blood is forced from the capillaries into the alveoli and so through the bronchioles, bronchi and trachea to discharge through the nose and mouth. As this discharge contains varying quantities of tubercle bacilli the utmost care is required on the part of the embalmer.

In cases of *deformity* and *rheumatoid arthritis*, it is necessary at least to straighten the legs, although this cannot be accomplished by normal methods. The procedure is to incise the tendons forming the boundary of the popliteal fossa and secure a splint in position. This should never be done until after the embalming treatment, otherwise the loss of embalming fluid seeping from the severed tissues would interfere considerably with the operation.

The advantages of this hygienic treatment are apparent to the professional mind, but to the bereaved the psychological effect of a properly embalmed cadaver is very great indeed. The embalmer is concerned with the appearance equally as much as with sterilization, and it will be realized that the closing of the eyes and mouth, hair dressing, shaving (if a male), positioning, dressing and make-up of the body are points which are embraced in the treatment and make all the difference to the finished results. This technique also means that the deceased can be left as though peacefully sleeping in bed until the actual time of the funeral, thereby avoiding all the gruesome accoutrements of the death chamber.

Items ancillary to the expeditious treatment of the dead body, which is the embalmer's chief concern, are the early clearance by the attending physician and/or coroner in the case of subsequent inquiry, and/or the issuing of the disposal certificate by the Registrar concerned. Not infrequently a person dying on a Friday cannot be cleared as regards the Registrar until some time on the following Monday or Tuesday. In this lapse of time,

during which the embalmer runs some little risk of criticism if he operates, a most distressing state of affairs can develop, and all embalmers look towards the day when the necessary arrangements can be accelerated to facilitate more prompt attention to their work. When the death occurs in hospital, the procedure is similar. Certification and registration are the same, and when the hospital is equipped with a pathological laboratory and post-mortem room, facilities are usually granted for the embalmer to inject the subject before removal. When this is not possible or desirable, the funeral director removes the body in a sanitary shell to his own preparation room for treatment. It is quite a common practice for the deceased to be taken home and placed in a bed which has already been prepared.

The shell referred to is a properly constructed zinc-lined coffin used for the conveyance of bodies. It can be kept scrupulously clean and sanitary. The term "shell" is also used to denote an inner coffin of wood or metal fitted into an outer coffin or case. Its purpose is to safeguard against the seeping of liquids resultant from putrefaction, but with modern methods this precaution is quite unnecessary. Shells are sometimes compulsory in cases in which the body is to be sent abroad or interred in a vault or mausoleum. The term "cremation shell" is sometimes used to refer to the coffin covered with cloth or velvet often used for cremations. Very few regulations govern the construction of the coffin for this method of disposal and it is a noted fact that cremation is gaining more and more public support year by year.

CREMATION

This hygienic method of disposal offers advantages in over-populated Britain which are so obvious as to require only the briefest mention, and the sanitary-minded funeral director is its staunchest advocate. There are, however, other important considerations apart from space saving, perhaps the most significant of which is the general design and lay-out of the present-day crematorium chapel. Here there is light, warmth and privacy which the mourners have every right to expect but seldom get in the average cemetery chapel, and this contrast must have contributed much to the choice of cremation as a means of disposal. Take too, the striking difference between the graveside scene with the grave diggers hovering behind a mound of damp earth, ready to fill in the grave as soon as the last mourner has left the temporary stage erected over the excavation, the whole intimacy of the procedure of seeing loved ones being lowered into the ground at the committal being exposed to the inquisitive, compared with the quiet courteous efficiency found at the crematoria. The effect of the privacy of the service rooms and tastefully planned gardens on the psychological, æsthetic and physical comfort of the relatives must be immense. The principals of our crematoria are to be congratulated on their foresight and courage in the strong part they have played in lifting the disposal of the dead from the macabre to the dignified.

There are some who consider cremation the alternative to embalming, but this is not so. Cremation is the alternative to burial, and the funeral director is concerned with the same problem in each case—prevention of putrefaction before the disposal of the remains. Although on the whole cremation can be more expeditious than burial, the more thorough examination and certification takes time, and it is extremely difficult to decide whether or not a body will keep for any certain period. Although I have had personal experience of some 26,000 cases, I would hesitate without first viewing the body, irrespective of the cause of death, to venture an opinion as to which case would or would not keep, for although it is generally accepted that any person dying a violent death or in a state of fever, particularly during the warmer weather, will become decomposed more rapidly than those dying consequent upon the processes of senility, it is my opinion that the conditions usually attributed to regulating the rapidity of the putrefactive processes are not necessarily associated with any particular cause of death, warmth or humidity, or with delay in disposal. Simple "heart" cases during the coldest weather have often become swollen with tissue gas in a matter of up to six hours after death, whilst even in the hot, humid atmosphere of July and August those dying as a result of puerperal and other fevers, suicides of many types, including drowning and carbon monoxide poisoning, have been kept in such conditions, without embalming, for a period of five or six days without becoming offensive in any way. Although it is readily acknowledged that it is not usual in the aggregate to encounter such conditions as the foregoing, there would appear to be a field for clinical inquiry into the causes of decomposition other than the accepted versions we now know.

Of recent years the question of the sanitary preservation of the dead has interested a number of ships' surgeons associated with shipping companies on the South American, Far East and Australasian runs, and it has been my privilege to give over sixty demonstrations to those desirous of tuition so that they would be capable of embalming those dying at sea and so bring them home for disposal. Many cases can be cited of the embalmer rendering signal service to the medical profession and in the course of justice. The following are worth quoting:—

During the recent war one London hospital had so many patients dying during an influenza epidemic that they could not all be accommodated in the refrigerator, and during the night rodents gained an entry into the mortuary and facially disfigured many of those bodies that had been left unprotected. To avoid any possible distress on the part of the relatives, the bodies were thoroughly embalmed, and then by means of "derma surgery" it was possible to rebuild the damaged tissues so that no evidence of disfigurement could be observed.

Another incident of medico-legal interest was an abortion case in 1940, in which the body had been concealed in an inverted position in the wardrobe for some weeks. Following a post-mortem examination the body had to be embalmed and the face restored to make it possible to identify the deceased. It is interesting to note that the body was identified within a few hours of the completion of the procedure.

THE CONFIRMATION OF DEATH

There is another matter on which some doubt exists—that of opening an artery in accordance with instructions under a will to ensure the death of the deceased before burial. The vessel invariably used, probably by reason of the ease and convenience with which it can be located and incised, is the radial artery and yet, surprisingly enough, one rarely finds the artery ligated following incision: therefore if the arm is placed by the side of the body, a considerable amount of blood is invariably found saturating the bed, whereas if the arm is placed on the abdomen, leakage from the vessel seldom occurs. This matter is almost automatically taken care of by the embalmer.

It must be pointed out that in the application of the embalming treatment to his cases, the funeral director considers that he is rendering a public service and as such no account is taken of the financial status of his clients, the service being available to rich and poor alike. This policy has its obvious advantages in so far as it acts as an insurance against being called out at some inconvenient hour to close or remove a coffin, and permits the funeral arrangements to be carried out without the constant worry of the body becoming offensive in any way.

CONCLUSION

The development of embalming in Great Britain is largely due to the British Institute of Embalmers Incorporated, a body formed in 1927 to promote and encourage the adoption of embalming as a sanitary measure before disposal. It is an examining and educational organization, membership being available only to those who successfully pass the rather high standard demanded by its Examining Board. It has a membership of some 600 in England and abroad. In Britain it is divided into areas or divisions, enabling its members to meet and discuss their problems and receive papers and lectures on such subjects as pathology, bacteriology, forensic medicine, and so on, from qualified lecturers. In recent years it has created a Research Board to inquire into the problem of any dead body being a potential danger to the living and, this proved, to ensure that the embalming treatment as applied is as thoroughly efficacious as it is claimed to be. The National Association of Funeral Directors is a body organized to deal with corporate effort on matters concerning its members on both a local and national basis. It, too, has an educational programme concentrating on the legal aspects of the disposal of the dead as concerns the funeral director: transportation, costings, development, the planning of suitable premises, and equipment, and so on.

EUTHANASIA

By A. LESLIE BANKS, M.D., F.R.C.P., D.P.H., *Barrister-at-Law.*

Principal Medical Officer, Ministry of Health.

It is customary to ascribe the changes of the present time to the industrial revolution, but it is worth considering whether this is, in fact, true. The oppression of the feudal system caused, from time to time, armed revolt among the subject peoples. Side by side with these bloody upheavals, of which the French revolution is the classic example, there proceeded a silent revolution infinitely more potent and of which we only now begin to see the outlines. The industrial revolution with its aggregation of masses in urban communities merely speeded up a process started several hundred years ago. With the invention of printing began that general dissemination of knowledge which is now consciously cultivated under the title of education. At the present time it is reasonably true to say that although the mass of people can read and write they still lack that critical faculty whereby a statement can be analysed and judged upon its merits. Herein lies the success, and danger, of the modern propaganda machine. On the other hand, although the critical faculty is not yet fully developed there has been a loosening of reliance on inherited wisdom, whether in the shape of the teaching of the Church or in folk lore. In the main the results have so far been beneficent in that the pressure of public opinion has been directed into the channels of social welfare. This is shown by the attention paid to sanitary measures, housing and social legislation of all kinds. The more sinister aspects are to be seen in the conflicting ideologies which have already produced two world wars in this century and now appear to threaten a third. Such fundamental changes in the public outlook have raised, as might be expected, a crop of subsidiary problems, many of which have become transmuted from the academic to the practical by modern scientific discoveries. Sterilization, birth control and artificial insemination are as significant indices of this revolution as the changed outlook towards abortion, illegitimacy, corporal punishment, suicide and capital punishment.

One of the most interesting manifestations of this changed outlook may be seen in the attitude towards the termination of life epitomized in the word euthanasia. Although of Greek origin (*eu* = well, *thanatos* = death) the term does not appear to have been used in classical Greek but it is mentioned by Cicero¹. The word first appears in English in its original meaning of a gentle easy death. Bishop Hall² in 1646, commends "To thee, my sonne, this true spiritual meanes of thine happy euthanasia", but the term must have been in common use by then for Ben Jonson³ wrote: "Dare I profane so unreligious be, to greet or grieve her soft euthanasie". In 1633 the Earl of Manchester⁴ referred to Augustus Cæsar who "So oft as he heard of a man that had a quick passage, with little sense of paine, he wished for himself that Euthanasie". From a quiet and easy death the definition changed to the means of bringing about a gentle and easy death. At first figurative (as used by Hume in his "Essays" in 1742: "Absolute monarchy is the easiest death—the true euthanasia of the British Constitution") it became transferred to its modern meaning

of the action of inducing a quiet and easy death. It is so defined in the New English Dictionary which continues: "used especially with reference to a proposal that the law should sanction the putting painlessly to death those suffering from incurable and extremely painful diseases".

The subject seems to have been first debated in its modern sense in the seventies of the last century. *The Fortnightly Review* (Feb., 218), and *The Spectator* (22 Feb., 240) of 1873, both carried articles on the subject and the latter journal went so far as to say that euthanasia would be no more demoralizing than capital punishment. Some indication of the interest in the new movement may be gained by the number of new words coined. An advocate of euthanasia became an euthanasiast. References appeared to euthanasian homicide and to subject to euthanasia became "to euthanatize". That the enthusiasm was not entirely one-sided may be judged from *The Spectator* of 1873 (22 Feb., 241/1): "I saw a crab euthanatizing a sickly fish, doubtless from the highest motives". These discussions were, however, theoretical, and in the words of the Hon. Lionel Tollemache in the *Fortnightly Review* already quoted: "he was in no wise ambitious of introducing a practical scheme of euthanasia among the subjects of Queen Victoria". He merely wished to discuss the subject philosophically as a preliminary to reform in some later age.

In November 1931, Dr. C. Killick Millard gave a Presidential Address to the Society of Medical Officers of Health on the "Legalization of Voluntary Euthanasia"⁵. Dr. Millard subsequently became honorary secretary of the Voluntary Euthanasia Society, and the movement in favour of euthanasia reached its peak in 1936 when a Bill was introduced into the House of Lords to legalize voluntary euthanasia in certain types of cases. This Bill was defeated but it is clear from subsequent discussions, for example, that of the Medico-Legal Society in March 1940⁶, that had it not been for the outbreak of war the subject would have been pursued vigorously. It can only be a matter of time before the question comes up for discussion again, and it may therefore be opportune to review the present position.

THE LEGAL POSITION

The artificial termination of human life is a matter which concerns all sections of the community and it is first necessary to examine the legal position. This is unequivocal. The killing of a human being by a human being is in law known as homicide. Homicide may be culpable, justifiable or excusable, but neither of the latter qualifications applies to euthanasia. Culpable homicide is a felony at common Law and may be either murder or manslaughter. Consider the definition of murder: "It is murder for a person of sound memory and discretion unlawfully to kill any human creature in being and under the King's peace, with malice aforethought, either express or implied by law provided the person killed dies of the injury inflicted within a year and a day of the same"⁷. Manslaughter is the unlawful killing of such a person without malice either express or implied. Be it noted that in both murder and manslaughter the criminal act may be one of omission as well as of commission.

Two points require special mention. When it has been proved that one person's death has been caused by another, there is a *prima facie* presumption of law that the act of the person causing death is murder unless the

contrary appears from the evidence either for the prosecution or for the defence. The onus is upon such person when accused to show that his act did not amount to murder. Malice aforethought, whether express or implied by law, must not be interpreted in its popular meaning. In law, express malice exists when the deliberate purpose of the accused is to deprive another of life or to do some great bodily harm. It is unnecessary to show any intention to kill the deceased person in particular or any special degree of ill-will towards him. It is hardly necessary to add that anyone who kills another person upon the desire or command of the latter is guilty of murder⁸. Incitement to suicide, if successful, is also murder. It is clear beyond all doubt that "the action of inducing a quiet and easy death" is in law murder. The fact that a jury might bring in a verdict of not guilty in a particular case does not alter the legal position.

The Voluntary Euthanasia (Legalization) Bill, 1936.—It is to the overcoming of this uncompromising definition that the efforts of the supporters of voluntary euthanasia have been directed. Those efforts have so far been concerned only with a small section of people, i.e. adults of sound mind suffering from an incurable and painful disease. The Voluntary Euthanasia (Legalization) Bill was introduced into the House of Lords on December 1, 1936, by Lord Ponsonby. He gave the purport of the Bill in the words of Lord Moynihan, who had recently died: "Briefly our purpose is to obtain legal recognition for the principle that in cases of advanced and inevitably fatal disease, attended by agony which reaches, or oversteps, the boundaries of human endurance, the sufferer, after legal enquiry and after due observance of all safeguards, shall have the right to demand and be entitled to receive release". The Debate is reported in *Vol. 103 Hansard (Lords)* p. 466 and is well worth reading. It is a good example of the value of the Second Chamber in discussion of important non-political issues. The Government of the day was content to leave the principle to the House, and Viscount Gage, on behalf of the Government, merely pointed out that the Bill would place various duties and responsibilities on the Minister of Health and that opinion among the doctors was divided.

The main opposition to the Bill came from the Roman Catholic and Anglican Churches and from the two leaders of the medical profession, Lord Dawson and Lord Horder. Viscount Fitzalan of Derwent put the case from the Roman Catholic viewpoint and was uncompromisingly against the Bill. The Lord Archbishop of Canterbury was less forthright, but he said: "I cannot but think that it is better to leave this most difficult and delicate matter in the hands of the medical profession, exercising its intimate and responsible judgment, rather than, as this Bill would propose to do, to drag it into the open and regulate it by elaborate official procedure". The most impressive opposition to the Bill came from the two medical members of the House. Lord Dawson pointed out that it was not correct to say that most cases of cancer were characterized by agonizing pain.

Lord Horder said that he was a little sorry that medical men had joined in this movement: "Into this matter of putting an end to life surely a new principle enters and I submit that this principle is outside the doctor's reference . . . Be it observed that the good doctor is aware of the distinction between prolonging life and prolonging the act of dying. The former comes within his reference, the latter does not". He reminded their Lordships that inevitability of a disease is never more than an estimate based upon experience: "How fallacious experience may be in medicine only those who have had a great deal of experience fully recognize". He endorsed Lord Dawson's statement that "we have never possessed so many means of relieving pain as we do to-day, and these means may be expected to increase in the future". He also criticized the condition of the Bill relating to the need for soundness of mind on the part of the patient, and finally, he pointed out the need to distinguish between the agony of friends and the agony of the patient: "To live is his, and not their, inalienable right".

The Bill was defeated by 35 votes to 14. Why did it fail? First, I think, because it was too rigid and inhuman in its requirements. The safeguards of the Regulations made under the Cremation Act cannot readily be applied to the living. The viewing of a dead body by a second doctor disturbs neither the dead nor the relatives. The referee, when in doubt, directs his questions to the doctors and, if not satisfied, orders a post-mortem examination. There is no delay and the whole procedure is carried out with the minimum of distress to the relatives. To introduce machinery such as this into the sick room, with solemn applications by the patient in writing in a prescribed form in the presence of two witnesses, certificates by two medical men and a personal interview with the referee would, for most people, produce an atmosphere quite foreign to all accepted notions of dying in peace. The patient would suffer final extinction at the hands, not of his own doctor, but of those of a stranger and in the presence of an official witness. Secondly, the Bill placed too much emphasis on the combination of pain and incurability. Neither of these criteria is capable of precise and final definition, and indeed if each case had to be argued in open court there would be conflict of medical opinion in practically every instance. But the principal reason for the failure of the Bill lay in the fact that public opinion and even the most informed minds were not ready to support it.

PRESENT-DAY OPINION

What is the position to-day? Have our views changed as a result of the past six years of war? Has the post-war dominance of the State in the everyday life of the citizen altered the position? How have the recent great advances in medicine affected the issue? All these questions require examination. The patient, his relatives and friends, the Church and the State all claim an interest in the subject. Last, but not least, the viewpoint of the doctor responsible for the patient's care must be considered.

Among those residual rights recognized by custom and the common law is the right of the individual to live his allotted span. The penalties for destruction of that life are known to all and the exceptions laid down with meticulous precision. Even the suicide must risk a verdict of "unsound

mind" by his fellow citizens on the jury. It is certain that the mass of the people would not to-day accept the legalization of euthanasia. Family ties are still the most dominant influence in English life, and the desire that the sick person should be left in peace is the uppermost consideration. Indeed, there is an instinctive feeling that the legalization of euthanasia might lead to an alteration of moral standards, particularly as regards the value of human life, and be a source of family feuds and discords after death. The interest of Church and State are less easy to define. The attitude of the Roman Catholic Church remains uncompromisingly against euthanasia in any form. The Anglican Church leaders appear to be divided but it seems clear that if forced to a decision, the majority would agree that, in accordance with Christian teaching, a man's life belongs to his Creator. As his Honour Judge Earengay pointed out in his valuable paper to the Medico-Legal Society on the subject of euthanasia⁶, the State has made a very considerable investment of capital in respect of each of its citizens. It is therefore entitled to an interest in each person's further usefulness, and in particular the decision, whether, and if so when, his life should be terminated. There is also the more general interest in the effect of such a changed outlook on public order and morality. But the State is, in fact, conditioned by public opinion. In a national emergency a Government must act in advance or even in opposition to the bulk of public opinion in the country. But in peace time no government acts in this manner. Every measure introduced has at least a majority of the people in support. On such an issue as this, it is probable that, as in the recent debate on capital punishment, the matter would be left open to the House to decide.

MEDICAL ASPECTS

It has been said that many doctors practise euthanasia daily in their work and some doctors have openly boasted of this. Is this true of the majority of the profession? If it is true, to what extent is legalization of the practice justified? It is twelve years since the Bill to legalize voluntary euthanasia was introduced. In that time the frontiers of successful therapy have been pushed far forward. Improved technique in surgery, readily available blood transfusion, improvements in anæsthesia, the discovery of penicillin and the sulphonamides all help to produce results far in advance of those possible twelve years ago. To give only one example, the results of operation on carcinoma of the rectum at special centres such at St. Mark's Hospital now promise cure even in very advanced cases. The success of stilbæstrol in carcinoma of the prostate makes it reasonable to suppose that similar substances, perhaps in conjunction with surgery and radiotherapy, will provide the answer to those "incurable" carcinomas which were primarily in the minds of the promoters of the Euthanasia Bill. It is true that the problems of many of the chronic medical diseases still remain unsolved. But those who have had most to do with this type of case know that an experienced medical

and nursing staff aided by physiotherapy and occupational therapy can so improve the condition of the patient as to effect at least partial cure. Above all, it is possible so to improve the mental outlook of these patients that life becomes worth living again⁹.

Mental disease is slowly responding to conquest. The results of malarial treatment in general paralysis of the insane and of the various forms of shock therapy are well known. The section of nerve tracts within the central nervous system is, as yet, in its infancy. Even so, a recent note by the peripatetic correspondent of the *Lancet* is not without significance. It read:—

"What goes on in the schizophrenic mind? This brilliant undergraduate and minor poet had been in catatonic stupor for nearly eight years lying in bed with his knees flexed and his head raised off the pillow, staring and speechless. For the last year he had been tube-fed. Then his frontal lobes were cut and he began to eat. Another six months elapsed before he spoke; quietly, slowly, condescendingly, but sensibly. When I met him he was reading, sitting in his wheelchair with ankylosed knees. One is always struck by the solemn preoccupation of these people, and I could not refrain from asking him eventually: 'Have you got your sense of humour back?' 'I don't think I ever lost it', was his smiling reply."

It seems clear that we are moving away from, rather than towards, the position defined by Sir Thomas More in "Utopia" wherein he said:—

"If the disease be not only incurable, but also full of continual pain, and anguish, then the priests and the magistrates exhort the man, seeing he is not able to do any duty of life, and by overliving his own death is noisome and irksome to others, and grievous to himself, that he will determine with himself no longer to cherish that pestilent and painful disease".

The art of medicine is to seek to cure, and failing this to alleviate. It will need a revolutionary change in the minds of the profession and of the public at large before the doctor is recognized in law as an executioner. Public opinion might consent to the destruction on compassionate grounds of the monster, the congenital idiot, and those rare and terrible progressive familial degenerations of the nervous system. A case could also be made for the inclusion of the final stages of dementia, and in particular of senile dementia, but intolerable pain is a challenge to the medical profession. It is not, in itself, sufficient to justify death.

In various discussions on euthanasia it has been pointed out that mental pain can be far more terrible than physical suffering. Mr. H. H. Greenwood in a discussion on "Euthanasia and the Psychoses"¹⁰ said: "Mental pain may be sufficiently dreadful as a concomitant of physical illness but the mental pain of the psychopathic and the insane is a *terra incognita* explored only by the psychiatrist and probably outstrips in intensity any physical suffering". He asked whether the term "voluntary euthanasia" excludes those who are demonstrably insane and who not only seek death but demand it. That physical pain should be controlled is now accepted by everyone and the means are available to do this. That mental pain is not sufficient ground for the termination of life was the agreement reached at

the discussion referred to. The fact that certain diseases are incurable is, in itself, no justification for the introduction of legislation on euthanasia. The traumatic paraplegic and the advanced rheumatoid arthritic can, and do with modern aids, lead happy and useful lives. The cripples, and in particular those disabled by poliomyelitis, can be helped to overcome their disability. The blind and the deaf can compete on almost equal terms with their fellows. Physical disability is a relatively minor matter provided that the will to survive and overcome it is present. Between the extremes of amentia and dementia and the incurable but not fatal diseases there is the group of killing diseases such as cancer and tuberculosis. The latter can be ruled out of this discussion both by reason of its response to treatment and the fact that if and when it decides finally to strike its victim down it does so quietly and painlessly. Prevention is the primary consideration in this disease and it presents no demand for euthanasia. Malignant disease is the cause of great suffering both to patients and relatives, but much can be done to relieve the distress of the patient going downhill. An efficient home nursing and domestic-help service, now made possible by the National Health Service Act, would also do much to relieve the strain on the relatives and give them the opportunity, so earnestly desired by the vast majority of people, of being of service to the stricken member of the family. Improved hospital services, with facilities for early diagnosis; treatment in special centres, and privacy for the advanced case, open up more profitable fields of endeavour than the final admission of failure implied in the legalization of euthanasia.

Even when everything has been done that can be done, the public will be content to accept the view of Lord Horder when he said: "We know that it is well within the ambit of the doctor's conscience to see that the fight is not too hard to be borne". The Courts are quick to defend the doctor in his professional relationships with his patient but the ancient legal maxim¹¹ still holds good "*Natura non facit saltum; ita, nec lex*".

I should like to express my indebtedness to the librarians of the Royal Society of Medicine and the Ministry of Health for their help. It is hardly necessary to add that the opinions expressed in this article are my own and do not necessarily represent the views of my Department.

References

- ¹ Cicero, *Ad Atticum*, xvi, 7, quoting Atticus.
- ² Balm. *Gil.*, 337.
- ³ Underwood, *Eupheme* ix.
- ⁴ *Al Mondo*, 164.
- ⁵ "The Legalisation of Voluntary Euthanasia" (1931) *Pub. Health, Lond.*, 45, 39.
- ⁶ Earengay, W. G. (1940): *Med.-Leg. Criminol. Rev.*, 8, 91.
- ⁷ Halsbury's Laws of England, 2nd edition.
- ⁸ *R. v. Sawyer* (1815): I. Russell on "Crimes", 8th edition, 618.
- ⁹ Banks, A. L. (1945): *Min. Hlth. Bull.*, 4.
- ¹⁰ "Euthanasia and the Psychoses" (1939): *Lancet, Lond.*, ii, 199.
- ¹¹ *Co. Litt.*, 238.

VACCINATION AGAINST SMALLPOX

By E. T. CONYBEARE, M.D., F.R.C.P.

Medical Officer, Ministry of Health.

ON July 5, 1948, the Vaccination Acts providing for the compulsory vaccination of infants ceased to have effect and vaccination against smallpox became voluntary, as is immunization against diphtheria. The National Health Service Act 1946 requires every local health authority, that is, every county and county borough council, to make arrangements for the vaccination of all persons resident in their area, and to give every medical practitioner providing general medical services under Part IV of the Act an opportunity to carry out vaccinations under Section 26 of Part III. All practitioners entering into arrangements with local authorities under this section (whether they also provide general medical services or not) will be able to obtain free supplies of the vaccine lymph which is distributed from the laboratories of the Public Health Laboratory Service. Books of the official printed application forms will be sent by laboratories to practitioners named by local authorities as having agreed to take part in the arrangements for vaccination, and in this way lymph will be issued as rapidly and directly as possible to prospective users. The return to local authorities of cards recording each vaccination and its result will entitle practitioners to receive an agreed fee per record. At the time of writing the amount of this fee, which is subject to negotiation, has not been settled.

The technique now officially recommended for all vaccinations and re-vaccinations is known as *the multiple pressure method*. Memo 312/Med. of the Ministry of Health (H.M.S.O. 1948, price 2d.), recently issued, gives illustrated details of this method, which has been in general use in the United States for some years. It is believed to have several advantages, e.g., it is almost completely painless, involves a minimum of trauma, and is unlikely to cause severe local reactions or septic complications. The essential features are the placing on the skin at the chosen site, usually the left deltoid region, of a drop of vaccine lymph covering an area about one-eighth of an inch in diameter, and the use of a fairly large straight needle which is either flat-sided or triangular in section. The needle is held parallel or tangential to the arm throughout the vaccination and the point is pressed firmly and rapidly on to the skin through the drop of lymph about thirty times within ten seconds, the whole needle being lifted clear of the drop each time in a plane perpendicular to the skin. By this means the needle point is not driven into the skin but at each "pressure" a little of the epidermis is pulled over it by the natural elasticity of the tissues. In this way the virus-bearing lymph is carried with a minimum of trauma to the deeper epidermal layers where multiplication takes place most easily. When the needle pressures have been completed the excess vaccine lymph is gently

wiped off the arm with sterile (not antiseptic) gauze or cotton-wool, the remainder being allowed to dry. If the needle is properly aligned little pain and no bleeding are caused; within a few hours there is no visible evidence of trauma, so that no immediate dressing is required. In using this method there are certain special considerations relating to the age of the subject and to whether the vaccination is primary or otherwise.

PRIMARY VACCINATION OF INFANTS

This should be regarded as a routine preventive measure of considerable importance to the individual as well as to the community. Although no longer prevalent or endemic in this country, smallpox still exists elsewhere, and there are few children born in Great Britain for whom at some time in their lives (e.g., as a result of an obligation to undertake military service or foreign travel) the protection afforded by vaccination will not eventually become essential. In explaining to parents the advantages of primary vaccination in infancy it is useful to point out that a first vaccination done at school age or later, by which time it may have become urgently necessary, is more likely to be followed by a severe local reaction or other complication than is a first vaccination done in infancy. Moreover re-vaccination, which is necessary for various reasons in later life, is an almost completely safe and simple procedure which can be faced with equanimity by persons successfully vaccinated in infancy.

Babies should not be vaccinated during the first few weeks of life while feeding from the breast or bottle is being established. Probably the best age in a thriving infant is about four months. Eczema is an important contra-indication to the vaccination of infants and, incidentally, great care should be taken to avoid the contact of any person who has been recently vaccinated with an eczematous infant in the same household, as such infants are liable to become infected and to develop a severe generalized form of vaccinia known as *eczema vaccinatum*. It is wise to postpone vaccination in any child with septic skin lesions or when there is known or probable exposure to infectious diseases such as measles and whooping-cough.

Infant vaccination should always be done on the arm, preferably on the lower posterior border of the deltoid muscle where scarring is relatively unnoticeable. Vaccination on the leg, sometimes demanded for æsthetic reasons, is undesirable because the local lesion tends to become infected. A single area of insertion is regarded as sufficient for the routine primary vaccination of infants but, when there has been exposure to smallpox, an attempt should be made to obtain a "take" on two areas of skin at least an inch apart. When the method described above is used the number of needle "pressures" to the selected skin area should be about thirty.

PRIMARY VACCINATION AFTER INFANCY

A first vaccination should only be done at these ages when there is exposure to or risk of smallpox, an obligation to serve with the armed Forces, or a

VACCINATION AGAINST SMALLPOX

By E. T. CONYBEARE, M.D., F.R.C.P.

Medical Officer, Ministry of Health.

ON July 5, 1948, the Vaccination Acts providing for the compulsory vaccination of infants ceased to have effect and vaccination against smallpox became voluntary, as is immunization against diphtheria. The National Health Service Act 1946 requires every local health authority, that is, every county and county borough council, to make arrangements for the vaccination of all persons resident in their area, and to give every medical practitioner providing general medical services under Part IV of the Act an opportunity to carry out vaccinations under Section 26 of Part III. All practitioners entering into arrangements with local authorities under this section (whether they also provide general medical services or not) will be able to obtain free supplies of the vaccine lymph which is distributed from the laboratories of the Public Health Laboratory Service. Books of the official printed application forms will be sent by laboratories to practitioners named by local authorities as having agreed to take part in the arrangements for vaccination, and in this way lymph will be issued as rapidly and directly as possible to prospective users. The return to local authorities of cards recording each vaccination and its result will entitle practitioners to receive an agreed fee per record. At the time of writing the amount of this fee, which is subject to negotiation, has not been settled.

The technique now officially recommended for all vaccinations and re-vaccinations is known as *the multiple pressure method*. Memo 312/Med. of the Ministry of Health (H.M.S.O. 1948, price 2d.), recently issued, gives illustrated details of this method, which has been in general use in the United States for some years. It is believed to have several advantages, e.g., it is almost completely painless, involves a minimum of trauma, and is unlikely to cause severe local reactions or septic complications. The essential features are the placing on the skin at the chosen site, usually the left deltoid region, of a drop of vaccine lymph covering an area about one-eighth of an inch in diameter, and the use of a fairly large straight needle which is either flat-sided or triangular in section. The needle is held parallel or tangential to the arm throughout the vaccination and the point is pressed firmly and rapidly on to the skin through the drop of lymph about thirty times within ten seconds, the whole needle being lifted clear of the drop each time in a plane perpendicular to the skin. By this means the needle point is not driven into the skin but at each "pressure" a little of the epidermis is pulled over it by the natural elasticity of the tissues. In this way the virus-bearing lymph is carried with a minimum of trauma to the deeper epidermal layers where multiplication takes place most easily. When the needle pressures have been completed the excess vaccine lymph is gently

inspection on the second day but by the seventh day vesiculation is marked and it will be obvious that the local lesion will go on to pustulation.

(b) *Accelerated or vaccinoid reaction.*—Some local reaction will probably be evident on the third day. Before the seventh day it has reached a maximum and shown vesicle formation, not, however, so marked as in (a) and not likely to lead to pustulation, although a small crust may form.

(c) *Precocious non-vesicular reaction.*—The local reaction is maculopapular, and reaches a maximum size on the second or third day. Before the seventh day it has subsided without the formation of a vesicle.

Occasionally a re-vaccination fails to produce any of the above results, and no local reaction is visible either on the third day or afterwards. In this event a repeat re-vaccination should be made with a fresh lymph.

RECORDING THE RESULTS

County and county borough councils have recently been advised by the Ministry of Health (in Circular 62/48) on the form of record to be required of practitioners who do vaccinations under Section 26 of the National Health Service Act. The suggested form of record is reproduced below.

MINISTRY OF HEALTH CIRCULAR 62/48

APPENDIX B

VACCINATION RECORD CARD

[Size Bins. by 5 ins.]

NATIONAL HEALTH SERVICE ACT, 1946 RECORD OF VACCINATION OR RE-VACCINATION		(For printing name of Local Health Authority)		For use by L.H.A.																									
PARTICULARS OF PERSON VACCINATED																													
Surname		Christian Name(s)		Sex*																									
				M. F.																									
Address		Vaccination done at		Date of Birth																									
				Day Month Year																									
				Primary Vaccination *																									
				Re vaccination *																									
NOTES			Particulars of Vaccination																										
* Put X in appropriate space. † This type of local reaction is sometimes described as "Reaction of immunity" ‡ If on first attempt at vaccination or re-vaccination no local reaction is obtained on 3rd day or later this should not be regarded as indicating complete immunity or insusceptibility, and at least one further attempt should be made with a fresh lymph. —See Also Overleaf—			<table border="1"> <thead> <tr> <th></th> <th>1st</th> <th>2nd</th> </tr> </thead> <tbody> <tr> <td>Date of Vaccination — — —</td> <td>Day Month Year</td> <td>Day Month Year</td> </tr> <tr> <td>Batch Number of Lymph — —</td> <td></td> <td></td> </tr> <tr> <td>Date of Inspection — — —</td> <td>Day Month Year</td> <td>Day Month Year</td> </tr> <tr> <td>Typical Primary Vaccina—7th-10th day</td> <td>*</td> <td>*</td> </tr> <tr> <td>Accelerated (Vaccinoid) Reaction—5th-7th day</td> <td>*</td> <td>*</td> </tr> <tr> <td>†Maximum Local Reaction—2nd-3rd day</td> <td>*</td> <td>*</td> </tr> <tr> <td>‡No Local Reaction — — —</td> <td>*</td> <td>*</td> </tr> </tbody> </table>				1st	2nd	Date of Vaccination — — —	Day Month Year	Day Month Year	Batch Number of Lymph — —			Date of Inspection — — —	Day Month Year	Day Month Year	Typical Primary Vaccina—7th-10th day	*	*	Accelerated (Vaccinoid) Reaction—5th-7th day	*	*	†Maximum Local Reaction—2nd-3rd day	*	*	‡No Local Reaction — — —	*	*
	1st	2nd																											
Date of Vaccination — — —	Day Month Year	Day Month Year																											
Batch Number of Lymph — —																													
Date of Inspection — — —	Day Month Year	Day Month Year																											
Typical Primary Vaccina—7th-10th day	*	*																											
Accelerated (Vaccinoid) Reaction—5th-7th day	*	*																											
†Maximum Local Reaction—2nd-3rd day	*	*																											
‡No Local Reaction — — —	*	*																											
When completed this card should be sent to (to be printed as required)			Signature of Doctor _____ Address _____																										

BACK OF CARD—provd space for (a) "NOTE OF ANY UNUSUAL LOCAL OR GENERAL REACTION OR OTHER SEQUELAE TO VACCINATION"
(b) Use by L.H.A.

It will be seen that space is available on this form for the results of the inspection of vaccination and re-vaccination to be recorded as already indicated and that provision has also been made for the result of a second attempt when necessary. Local authorities will ask for information to be given on these record forms about complications such as encephalomyelitis.

Patients who have been vaccinated or re-vaccinated because they intend to travel abroad often ask practitioners to complete the *International*

requirement to travel to areas where smallpox is likely or prevalent. In school children and adults the local and general reactions to a primary vaccination tend to be more severe than in infants. The risk of encephalomyelitis after vaccination is small at any age, much smaller than the risk of death run by the unvaccinated when exposed to smallpox, but it is probably least when primary vaccination is done in infancy.

When the primary vaccination of school children or young adults is necessary but not urgent it is probably best to use the multiple pressure method with a reduced number of needle pressures, say five to ten instead of the usual thirty. If exposure to smallpox is likely or suspected and therefore a successful "take" is essential, the full number of pressures should be made in each of the two areas an inch apart. It is preferable that *primary* vaccination should not be done at the same time as other preventive inoculations, e.g., against the enteric fevers, typhus, and the like. An anti-yellow fever inoculation should not be given within fourteen days before, or within three weeks after, a primary vaccination.

RE-VACCINATION OF CHILDREN OR ADULTS

The purpose of re-vaccination is to maintain or revive the immunity against smallpox conferred by a previous vaccination. Children primarily vaccinated in infancy ought to be re-vaccinated on entering and again on leaving school. Re-vaccination is usually done as a routine on entering the armed Forces and then repeated at intervals which vary with the circumstances, e.g., every five years when on home service and every two years when overseas. Doctors, nurses, sanitary inspectors and others likely to have to deal with cases of smallpox need regular re-vaccination at yearly intervals.

The multiple pressure method is particularly useful for re-vaccination because it allows maximum accuracy in the interpretation of the results. Up to thirty pressures of the needle in one area are sufficient except when there is known or probable exposure to smallpox which makes at least two separate areas of needle pressures advisable.

INSPECTION OF RESULTS

Primary vaccinations should be inspected between the seventh and the tenth day. By the eighth or ninth day the marked vesicle formation and beginning pustulation of typical primary vaccinia are unmistakable. When by this time there is no local reaction to primary vaccination, either a fault in the technique or loss of potency of the lymph should be suspected rather than insusceptibility to vaccination which is extremely rare, and at least one fresh attempt should be made with a new batch of lymph.

At least two inspections are required for an accurate assessment of the result of a re-vaccination. One should be on the second or third day after it has been done and the other about the seventh day. This double inspection of a re-vaccination will usually show one of the following three results:—

(a) *Typical primary vaccinia*.—No local reaction may be visible at the

HYDRAMNIOS

By J. P. BUSH, M.B., B.S., D.OBST.R.C.O.G.

Obstetrician, North Devon Infirmary, Barnstaple; Formerly Resident Obstetric Officer, St. Thomas's Hospital, London.

IN a normal healthy pregnancy the fœtus is surrounded in its amniotic sac by a clear fluid. This fluid, known as liquor amnii, serves several functions, and in the amniotic sac of a full-term healthy fœtus is about 1 to 3 pints (0.6 to 1.3 litres) in quantity. The condition of hydramnios, i.e., when this normal quantity is exceeded, occurs once in 100 to 200 pregnancies, and quantities of 15 and even up to 30 litres of liquor have been recorded.

ETIOLOGY

The mechanism of the production of normal liquor is much disputed and the production of hydramnios is imperfectly understood. In a field so full of theories it is difficult to assess the relative value of each.

Maternal conditions.—Multiparous women are more often affected than primigravidæ. Hydramnios occurs more commonly in association with some general disease or disturbance in the mother, e.g. diabetes mellitus, syphilis, leukæmia, anæmia. Browne (1946) states that the increased tendency to hydramnios in diabetics is believed to be due to the high concentration of sugar in the liquor amnii stimulating the amniotic epithelium to more active secretion. Apart from the fact that excessive degrees of hydramnios in diabetics are less often seen since the introduction of insulin, Browne gives no substantiating evidence for this belief.

Heart disease of the mother, particularly when there is congestive cardiac failure and generalized œdema, is often accompanied by hydramnios. Other conditions, e.g. lung, liver or kidney disease, which may predispose to general anasarca are often also complicated by hydramnios. The condition often occurs in association with a severe pre-eclamptic toxæmia.

Fœtal conditions.—Fœtal malformations are the most common of all conditions associated with hydramnios, and especially deformities showing the absence of closure of fœtal cavities, occlusion of the œsophagus or pylorus, hare-lip, anencephaly, hydrocephaly, spina bifida, and ectopia vesicæ.

Among the 780 cases delivered in the maternity unit of St. Thomas's Hospital in 1946 there were 9 cases of hydramnios recorded (an incidence of 1 in 86.6). Of these, fœtal deformities were present in six cases, i.e. 66 per cent. (anencephaly 2—one was combined with spina bifida and an umbilical hernia; hydrocephaly 1; spina bifida 1; diaphragmatic hernia 1; and abnormalities of fingers 1). The other 3 cases were unexplained, but in 2 of these there was a concurrent associated toxæmia of pregnancy.

Hydramnios occurs commonly in one and sometimes in both of the amniotic sacs of a uniovular twin pregnancy. This often arises at an early stage in pregnancy as occurred in case 2 (p. 118). Other disease of the child

Certificate of Vaccination against Smallpox which was introduced in 1944. This document requires the result to be stated in one of three terms, i.e., typical primary vaccinia, accelerated reaction (vaccinoid), or "reaction of immunity". By the last is meant the precocious non-vesicular reaction already mentioned (the implication as regards interpretation suggested by the term required in the international certificate is not necessarily correct). At present such certificates are valid for three years (a certificate which states the result of vaccination to be nil or "no reaction" is not acceptable). The existing position regarding this international certificate is unsatisfactory and it will form a subject for discussion at forthcoming meetings of the World Health Organization.

INTERPRETATION OF RESULTS

Doctors are sometimes asked to interpret the results of a vaccination. The following brief comments may be a useful guide:—

(a) *Typical primary vaccinia*.—This result, whenever obtained, means that the subject initially had no immunity to smallpox but will subsequently be protected for at least three years and possibly longer.

(b) *Accelerated or vaccinoid reaction*.—This will only be obtained after a re-vaccination. It means that initially there was an incomplete immunity to smallpox and that complete protection for three years or possibly longer will probably follow. The initial incomplete immunity may have been either the natural decline after some years of a complete immunity conferred by the previous vaccination or a consequence of using a lymph of poor immunizing power.

(c) *Precocious non-vesicular reaction*.—This is only seen after re-vaccination or in those who have had smallpox. It is commonly called "reaction of immunity", but this is unwarranted because in approximately ten per cent. of all persons subjected to re-vaccination a precisely similar reaction can be obtained with lymph which has been made non-potent by heat, and in them such a reaction might be merely evidence of sensitivity to some antigenic substance in the lymph and not of immunity to the living virus of vaccinia. Only when this result has been obtained in at least two re-vaccinations of a given individual using different lymphs, one or both of which have been shown capable of producing typical primary vaccinia in other individuals, is it wise to regard it as an index of a good immunity to smallpox.

(d) *No reaction*.—This should always lead to at least one further attempt with a different lymph, preferably one proved capable of producing typical primary vaccinia in other persons. Insusceptibility of infants or adults to primary vaccination is extremely rare. Even in those who have had smallpox it is unusual. The immunity to smallpox of those who show this lack of reaction is quite uncertain and, if they are in any danger of exposure to the disease, the best advice to give them is that they should be re-vaccinated repeatedly at intervals of six months or so until a definite response is obtained.

But in all cases of hydramnios there is either a larger area of mucous membrane through which the foetal serum can transude, or there is some other factor increasing the permeability of the amniotic epithelium, i.e. anæmia or anoxia. For example, in cases of anencephaly the open area on the skull will transude fluid. It has also been proved by de Snoo (1937) that the foetus *in utero* does swallow liquor which is absorbed. It is therefore not surprising to find large quantities of liquor in cases in which the foetus has a congenital closure of the œsophagus or stenosis of the pylorus.

Much further work requires to be done before the etiology of liquor amnii and hydramnios is fully understood, but I feel that the majority of evidence at present available does seem to point to a foetal origin.

CLINICAL TYPES OF HYDRAMNIOS

There are two main types of hydramnios, acute and chronic, although Browne (1946) classifies all cases of hydramnios in four groups: (1) Acute: this is very rare, and in his opinion every case, because of its rarity, justifies reporting. (2) Chronic. (3) Subacute (which Browne considers self-explanatory, although he does not differentiate it clearly from the chronic type). (4) Chronic, which becomes acute.

Except in uniovular twins, in which the acute type may occur as early as the 12th week of pregnancy, hydramnios rarely gives trouble before the 18th week. The chronic type usually makes its appearance in the later months of pregnancy.

Acute hydramnios.—This condition, which commonly begins about the fourth or fifth month of pregnancy, usually leads to spontaneous abortion if no treatment is instituted. The uterus rapidly increases in size, over the course of a few days, and may reach a size larger than a full-term pregnancy. Pressure symptoms occur early and are pronounced, such as pains in the back, abdomen and thighs, dyspnœa, a feeling of distension, nausea, and vomiting. Palpation of the abdomen reveals no information apart from an extremely tender uterus and a possible fluid thrill. Foetal parts are not palpable, and the foetal heart may or may not be audible. Striæ gravidarum occur with occasional small hæmorrhages into the skin.

On vaginal examination, the cervix is usually high up in the pelvis, which is an important differentiating point from ovarian cyst, is effaced, and often the external os is opened. Abortion usually terminates the condition before the sixth month, but if in a case of uniovular twins one foetus dies *in utero*, the other may survive and continue to term, spontaneous cure of the condition occurring.

Chronic hydramnios.—The course of the chronic type is much slower. The uterus gradually increases in size, and reaches a size much greater than that which would be expected by the length of the period of amenorrhœa. Premature labour is common, but abortion before the 28th week is infrequent. The condition may also occur in ectopic pregnancies which have not ruptured, or which have continued after rupturing, and in these

or placenta and membranes may be causative factors of hydramnios, especially those involving obstruction of the venous circulation of the fœtus, e.g. stenosis of the cord, stenosis of the aorta, syphilis or other placental disease.

Paternal conditions.—McFeeters (1939) has suggested that the male parent may have some responsibility for the causation of this condition. He has postulated that there is an hereditary incidence associated with fœtal malformations. To support his theory, he gives an example of a family pedigree in which the evidence is, at least, strongly suggestive of a familial tendency to anencephaly with hydramnios, transmitted by the male member. Baur, Fischer and Lenz (1939) also regarded anencephaly as a familial condition.

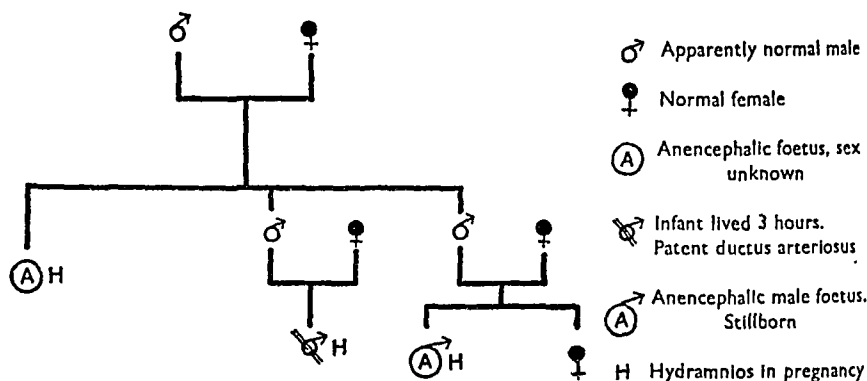


FIG. 1.—McFeeters' case: (1) In each case the mother was a primigravida, whereas generally 75 per cent. of cases of hydramnios occur in multiparæ. (2) The relationship in this family is entirely on the paternal and not the maternal side. None of the siblings of the three women had a case in their families.

Davenport (1920), in a study of 644 births in families in which twins had occurred, suggested that there was a greater tendency for twins to occur among the siblings of the father than of the mother of twins. If this is correct, it is equally possible that the paternal element in the production of hydramnios may be an essential feature.

Erythroblastosis and hydramnios.—These two conditions often occur together. This fact has been known for years, although the pathology of icterus gravis or hydrops has not been understood until recently. In cases in which the two conditions are concurrent, the liquor is a deep yellow colour, thus adding force to the suggestion that the origin of the liquor amnii is fœtal, either in part or entirely. A transudation from a fœtal circulation in which there has already been a certain amount of hæmolysis, and therefore the plasma of which contains bilirubin, would be icteric in tinge. In these cases the maternal serum is not icteric, and therefore if the liquor originated as a transudation from the maternal circulation, it would be normal in colour.

In all cases of hydramnios the mother need have no debilitating disease.

undue enlargement of the uterus. A history of Rhesus incompatibility or examination of the mother's blood by the Race-Coombs test may assist in diagnosis. X-rays may show the classical halo around the foetal head and body due to oedema of the subcutaneous tissues.

Concealed ante-partum hæmorrhage.—If the hæmorrhage has been severe, all the signs of shock due to blood loss may be present. The uterus is tender, and abdominal pain is usually more acute than the discomfort or pain associated with hydramnios.

PROGNOSIS AND DANGERS OF HYDRAMNIOS

It is rare for hydramnios to reappear in future pregnancies unless accompanied by a marked familial history of foetal deformities associated with hydramnios, as in McFeeters' case (1939).

The prognosis for the mother in a case of acute hydramnios is good. Abortion usually terminates the case early. In chronic hydramnios, apart from the added dangers to which the mother is exposed in labour, the prognosis is good. Dangers to which the mother is additionally prone are divisible into those before labour starts, and those during labour.

Before labour.—Cardiac collapse, respiratory failure, hydroperitoneum, and hydrothorax may occur. The ureters are more likely to be compressed, and therefore there is the added liability to hydronephrosis and inflammatory conditions in the pelvis of the kidney.

In labour.—Owing to the overdistension of the uterus, the first stage may be long, inert, and tedious. Prolapse of the cord, or of any of the limbs may occur when the membranes rupture and there is a sudden rush of amniotic liquor. Hydramnios also predisposes to malpresentations of any kind and to uterine inertia. On rupture of the membranes, the liquor may suddenly escape and abruptio placentæ occur. Post-partum hæmorrhage is common in cases with hydramnios, as the excessive distension of the uterus before labour predisposes to an atonic third stage.

Prognosis for the child.—In acute hydramnios, the prognosis for the child is bad, but except for foetal deformities and complications of labour, e.g. prolapsed cord, the foetal prognosis in chronic hydramnios is good.

TREATMENT

The treatment of *acute hydramnios* is abortion by letting off the liquor slowly in order to avoid shock. This usually occurs spontaneously. In critical cases in which the diagnosis is not certain a uterine sound may be passed through the os, as, if the case is really hydramnios, rupture of the membranes is the correct treatment.

The treatment of *chronic hydramnios* is more complicated. If there is any etiological factor which can be incriminated then the treatment of that condition, e.g. syphilis, diabetes, toxæmia, anæmia, should be instituted. If the symptoms are marked, the patient should be put to bed on a light diet. As soon as the heart appears to be affected, the liquor should be let off slowly in order to avoid shock from sudden decrease in intra-abdominal tension, to minimize the risk of abruptio placentæ, and to prevent prolapse of the cord or limbs. When the patient goes into labour, all preparations

cases the diagnosis is extremely difficult. Chronic hydramnios may also occur in a twin pregnancy in which usually only one sac is involved. In one of de Lee's (1943) cases the bag of waters over the internal os, felt per vaginam, was relaxed, whilst the uterus, felt per abdomen, was very tense, a fact which Rémy and Ahlfeld used for the diagnosis of hydramnios in the upper twin. This condition may cause great cardiac distress or renal insufficiency on account of the enormous distension.

In one of our cases at St. Thomas's Hospital in June 1946, at the 37th week of pregnancy the patient complained of severe dyspnoea, a feeling of distension, and pain under the right costal margin. The circumference of the abdomen at the level of the umbilicus was more than 46 inches. On high rupture of the membranes with a Drew Smythe catheter, considerably more than 9 pints of liquor were removed and measured. A fair quantity, estimated at about 1 to 2 pints, of liquor escaped when the child, an anencephalic monster, was born. This particular patient, a multigravida, had previously given birth to an infant at full term in 1934, which died of congenital heart disease. She had also been delivered of two other children, one of whom died of "pneumonia" at the age of eighteen months, and the other, born in 1937, is alive and well. It is not recorded whether or not the "pneumonia" was proved at post-mortem examination.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Hydramnios is usually first suspected by the observation that the height and size of the uterus do not correspond with the expected size for the period of amenorrhœa. Before the diagnosis is made it is necessary to confirm that the patient is pregnant. Because of its rarity the diagnosis is often made by a process of exclusion. The differential diagnosis of hydramnios should exclude the conditions listed below:—

Hydatidiform mole.—In this condition the uterus may be large for the dates, but almost invariably a patient with a hydatidiform mole complains of bleeding per vaginam, or at least of a blood-stained discharge. The demonstration of chorionic grape-like villi will establish the diagnosis of hydatidiform mole.

Retroverted gravid uterus, which has caused acute retention of urine. This is a common mistake, and the differentiation is easy by the passage of a catheter, thus relieving the retention. A vaginal examination would also clarify the picture. This condition usually occurs much earlier in pregnancy, i.e., about the 14th week.

Ovarian cyst.—If a patient with hydramnios is placed in the knee-elbow position, the fœtus can usually be balloted against the abdominal wall. Examination of a patient with an ovarian cyst usually discloses that the uterus is situated below the tumour and is not continuous with it. Per vaginam, the cervix is closed and firm. The usual pregnancy signs and symptoms are absent.

The case which gives the greatest difficulty in diagnosis is an acute hydramnios occurring in a patient who also has an ovarian cyst. Mrs. R., whose case history is given (case 2), page 118 was diagnosed before admission as either acute hydramnios or normal four-month pregnancy with an ovarian cyst. Radiological investigation of an abdominal tumour may give absolute proof of pregnancy with hydramnios after about the sixteenth week. However, it is often impossible, even with the help of X-rays, to be certain of the presence of a fœtus in a uterus with hydramnios.

Multiple pregnancy may cause excessive enlargement of the uterus. The palpation of two fœtuses or an X-ray will clinch the diagnosis.

Ascites.—Free fluid in the peritoneal cavity, and particularly a tuberculous localized ascites, may give rise to difficulty in diagnosis. No pregnancy changes will be noted, and usually in a case of ascites there is an area of tympany around the umbilicus or epigastrium.

Hydrops fœtalis, or fœtal œdema, due to erythroblastosis, may occasionally cause

fœtal heart tones audible. A swelling arose from the pelvis and reached up to three to four inches above the umbilicus. Her heart was mildly decompensated, and for this reason she was admitted for rest and observation, a tentative diagnosis being made of acute hydramnios. Another opinion given after admission suggested that the patient was pregnant and that she also had a large ovarian cyst.

On her fourth day in hospital, the patient passed spontaneously more than 3½ pints of amniotic liquor (measured), and the following morning aborted spontaneously. The original diagnosis of acute hydramnios was thus confirmed, the pregnancy being a uniovular male twin pregnancy. She passed also a considerable amount, probably more than two pints, of liquor at the time of abortion as well as draining continuously from the time of rupture of the membranes, a period of about eight hours. The total amount of liquor was, probably, therefore about 6 or 7 pints. The patient made an uninterrupted recovery, and has since been delivered by Cæsarean section (with other indications) of a live female child, apparently normal, at the 37th week of pregnancy. There was no hydramnios with this pregnancy and there was no cardiac failure or decompensation. She remained well throughout her pregnancy until a synpneumonic empyema sent her to hospital.

There is no family history here of either fœtal abnormality or hydramnios. The association of hydramnios with cardiac failure has been noticed before, and it is interesting that in her second pregnancy there was no cardiac failure, nor was there any excess of liquor.

Case 3.—Mrs. V., a primigravida of thirty years, expected her first child on December 14, 1941. She had a completely uneventful antenatal history until October 20, i.e., at thirty-two weeks of pregnancy. She then complained of severe distension of her abdomen, which had come on rapidly over the course of two days. There were no toxæmic symptoms, but she had considerable abdominal pain and signs of a urinary infection. On admission, a concealed accidental hæmorrhage was suspected with a complicating pyelitis. Two days later her condition deteriorated, and the abdominal distension was more marked. A diagnosis of acute hydramnios was made and confirmed by X-rays which also showed the fœtus to be anencephalic. Accordingly the membranes were ruptured with a Drew Smythe catheter, and the anencephalic monster delivered two hours later. She made a completely uneventful recovery, and has since been delivered of a normal child.

In each of these cases, the hydramnios occurred in the first pregnancy and was acute in onset. Constitutional disturbance was considerable, and in each case rupture of membranes, spontaneous or artificial, rapidly gave relief. The first two cases indicate the type of case with which one should be prepared to deal in a uniovular twin pregnancy, and case 3 is an example of acute hydramnios occurring late in pregnancy, which is usually associated with fœtal abnormality.

I wish to thank Mr. R. B. K. Rickford for helpful criticism and advice, and the Staff of St. Thomas's Hospital for permission to publish the details of cases 2 and 3.

References

- Abrams, A. A., and Abrams, S. B. (1946): *Amer. J. Obstet. Gynec.*, 52, 299.
 Baur, E., Fischer, E., and Lenz, F. (1939): "Human Heredity," London.
 Browne, F. J. (1946): "Antenatal and Postnatal Care," 6th edition, London.
 Davenport, C. B. (1920): *Amer. Naturalist.*, 54, 122.
 de Lee, J. B., and Greenhill, J. B. (1943): "Principles and Practice of Obstetrics," 8th edition, Philadelphia.
 de Snoo, K. (1937): *M Schr. Geburtsch. Gynäk.*, 105, 88.
 Gates, R. R. (1934): "Chances of Morbid Inheritance," London.
 Henkel, M. (1930): *Dtsch. med. Wschr.*, 56, 1249.
 Luttger, H. (1922): *M Schr. Geburtsch. Gynäk.*, 59, 35.
 McFeeters, J. W. (1939): *Brit. med. J.*, 1, 238.
 Marshall, G. B. (1914): *J. Obstet. Gynec. Brit. Emp.*, 25, 201.
 Polano, O. (1905): *Zbl. Gynäk.*, 29, 1203.

should be at hand for the correct treatment of uterine inertia. A forceps delivery may be indicated, and all preparations should be at hand to deal with a possible post-partum hæmorrhage.

De Snoo (1937) devised an ingenious method for treating hydramnios conservatively. He injected saccharin into the amniotic fluid to make the fœtus swallow a large amount of the fluid. By this means, in 20 cases he succeeded in overcoming polyhydramnios, thus enabling women to carry their pregnancies to term. Experiments by de Snoo proved that excessive liquor does not come from the fœtal kidneys but from the placenta and amniotic epithelium. Henkel (1930) recommended relieving the uterus by abdominal paracentesis, but de Lee and Greenhill (1943) believe this to be of only temporary benefit, as well as being very risky.

Abrams and Abrams (1946) reported two cases of hydramnios, occurring at the sixth month of pregnancy, which were successfully treated by the administration of ammonium chloride. This was given in $7\frac{1}{2}$ grain (0.5 gm.) enteric-coated tablets, 12 a day for nine days in one case, and 10 a day for seven days in the other. In both cases this treatment was satisfactory; the hydramnios regressed and did not recur. Both patients were delivered safely of normal infants at term.

Cases of acute hydramnios should be admitted to hospital and probably as an acute emergency; but cases of chronic hydramnios should also be confined in hospital, when possible, in view of the complications which may occur during labour.

ILLUSTRATIVE CASES

Case 1 (Marshall, 1914).—Mrs. G., a primigravida of thirty-one, was seen on March 7, 1913, by Marshall. He then confirmed that she was eight weeks pregnant, her period of amenorrhœa dating from her last menstrual period, January 1-5. On May 11, i.e., at the 18th week of pregnancy, she complained of sudden severe colicky pains in the lower abdomen and sudden distension of the abdomen. She remained in bed for two weeks in continuous pain. At this time her uterus was larger than an eight-month gestation, round in shape and deeper and broader. From the symphysis pubis to fundus uteri measured $11\frac{1}{2}$ inches, and the circumference of her abdomen at the level of the umbilicus was $32\frac{1}{2}$ inches. The uterus was fluctuant, tense, and very tender to palpation. Therapeutic abortion was proceeded with; the membranes were ruptured and five pints of liquor were collected, but more was lost. She was given injections of pituitrin, and digital evacuation of the remains of two macerated fœtuses was performed. Uniovular male twins were discovered, equal in size to a four-month fœtus, and only one amniotic sac was affected.

Case 2.—In December 1945, Mrs. R., a primigravida of twenty-five, was admitted to St. Thomas's Hospital at the 17th week of her first pregnancy, in the early stages of cardiac failure. Mitral stenosis had been diagnosed five years previously, and she had been in hospital once before, a year earlier, owing to her heart condition. The right side of her heart was known to be enlarged. She was seen a month after conception and was advised that the pregnancy be allowed to continue under supervision. The early weeks of her pregnancy were uncomplicated, although she never felt "on top of her form". At the 16th week she was seen, and complained of feeling unwell, with pains in her back, and she was vomiting. She was sent home to bed to rest, her lassitude being considered to be due to her heart condition. Six days later she was seen at the antenatal clinic again, when she complained of feeling "awful". Her backache was worse, in the bottom of her spine, and continuous, and she was sleeping badly. The vomiting had improved, but her abdomen had increased in size rapidly during the course of the last week, and she complained of severe dyspnœa on the slightest exertion. She also complained of a pain in the right side—"like a stitch"—and her backache seemed to prevent her from using her legs. She felt tired and useless and was unable to do anything. Her ankles swelled in the evening, but her cough had improved. On examination the abdomen was tense, and fluctuation could be elicited. No fœtal parts were palpable nor were

man, he devised, without any scientific knowledge, the best method ever evolved for reducing weight. (He himself weighed some thirty stone.) The diet is simple. He cut out all fat and every sort of sugar and starch. For his energy the patient uses up his own stores. It is an ample, pleasant diet. Any doctor can make out the list of what not to eat. Without any hardship weight can be reduced by half a pound a day, or a stone per month. The patient should weigh himself each week. He will know at once if he is keeping to his diet, and so will his doctor. The amount he should reduce varies with his initial weight. As a rule I have taken off two stone as a minimum, but in some cases as much as five stone has been removed to the patient's great delight.

Muscle toning.—The patient should be encouraged to do exercises each morning and evening. These tone up his muscles and are good for his heart. He should be urged to walk as much as possible. Above all he should be forbidden to use lifts. This last is the most difficult to make him observe. To enter a lift and press the button is almost irresistible—and no one will know! But lifting his own weight by his own muscles is the best thing for his heart. He can go up stairs as slowly as he likes, but he must walk. The elimination of his fat reduces his intra-abdominal pressure, which is what is desired.

Now a word about the advice so commonly given to these old people by their doctor and by the ordinary surgeon, that they must not risk an operation "at their age". We can presume that every form of truss has been tried—the double truss, the opposite-sided truss, so much vaunted at one time for these large herniæ, and the bag truss, which is the worst of all. None has met the requirements of the patient. Yet the surgeon still says that operation is out of the question, because that is the view he has been brought up to hold. He has never thought of any alternative, much less tried one. Over a certain age a patient is too old to be operated upon for hernia—that is an accepted axiom. But does the surgeon take the same view when the life of the patient has become burdensome from prostatic enlargement? No! In such cases old age is taken for granted, it is not even considered as a drawback. Prostatectomy was opposed, and for the same reason, when first introduced. Only when surgeons tried it and found it was worth while, was it accepted. But the two operations can hardly be compared in severity, in discomfort, in risk, or in the general upset of the patient.

OPERATIVE PROCEDURE

The operative problem is to close the ring and canal firmly, permanently, and rapidly, for the limited number of years left to the patient; that is all that is required. This can best be done by sewing up the ring, empty sac, and cord in one, with silver wire gauge no. 26.

A good anæsthetist is essential. He should see the patient beforehand and make up his mind as to the best method of rendering him unconscious for the ten minutes or quarter of an hour that is required for the operation; longer should not be necessary.

THE OLD GENTLEMAN'S HERNIA

By D. C. L. FITZWILLIAMS, C.M.G., M.D., CH.M., F.R.C.S.

Surgeon, Royal Masonic Hospital, and Mount Vernon Hospital for Cancer Research.

WE all know the old gentleman who has had a large uncontrollable hernia for years, which he refused to have operated upon in the early days, although it was even then difficult to find comfort with any form of truss. After many years' suffering, he went to his doctor again with the idea of getting it rectified, only to hear that it was now too late and that he was too old to have an operation with safety. Possibly if the doctor had previously advised operation and this had been refused, he may add that it was his own fault for not listening to him. Doctors are only human, and the temptation to say "I told you so" assails us all at times. There is, however, a method of operative treatment which, if carried out properly, can relieve these patients.

The patient is as a rule short, well over fifty-five, perhaps verging on seventy. He is a lot stouter than he likes; this is because he can take little exercise on account of his infirmity. If he does anything in a hurry, down comes the rupture. Any stumble or jolt may have the same awkward effect. Coughing nearly always brings it down, and he is a bit bronchitic every winter. When the hernia does come down he knows he must get it back at once. He has been warned about this. He has never forgotten how frightened he was, what torment he had, and how he sweated when it came down once and he could not get it back until the doctor came to his relief. He knows he had better lie down to reduce it, sometimes he can't reduce it otherwise. When he does get it back, it is difficult to adjust the truss without undoing most of his clothing. Even if he can retire to a convenient lavatory he can't lie down there. In the open he can lie down, but other considerations arise about undoing his clothing. Explanations are very awkward; as a result he does not go out much. Things go from bad to worse; he becomes a nuisance to himself and a pest to his family. Finally he may find that life becomes almost unbearable. I have depicted perhaps an extreme case, but most practitioners know the old fellow.

GENERAL TREATMENT

It used to be said that fat and the physician were the two great enemies of the surgeon. In the case of treatment of the uncontrollable hernia of the aged the physician's place is taken by the ordinary surgeon, but obesity is the most important factor. Excess of fat acts as a deterrent to operation in several ways; there is the flabby condition of muscle, the fat-encumbered heart, and the fat in the omentum which raises the intra-abdominal pressure. All these require attention.

Weight must be reduced.—This is difficult to achieve in the aged, who do not take kindly to dieting. Nowadays with rationing it is even more difficult.

The best way of reducing weight is by "Banting's diet" which was fashionable some thirty years ago when people "banted". Banting was the famous Paddington undertaker who lived more than a hundred years ago. Although quite an uneducated

A GLASS OF BEER ?

By C. G. LEAROYD, M.R.C.S., L.R.C.P.

"I SUPPOSE a glass of beer won't hurt me?" "What about a drop of stout to his dinner, doctor?" The practitioner is often asked such questions, which if he remembers his Latin he will recognize more often than not as "*num*" and "*nonne*" questions, in which the answers are implied, and although they are often put to him just as he is leaving the bedside, perhaps in the hope of obtaining a snap judgment, the careful physician will have already considered the matter many times and will pause only to apply the general principles involved to the particular case. In his mind will be the long-learned lessons from the physiological laboratory, *obiter dicta* from the tomes of Osler and Price, papal bulls from biochemistry which he may take like a good Protestant, the clear, authoritative voice from the little red book, "Alcohol, Its Action on the Human Organism," which bears the hallmark of the Medical Research Council, various odd articles, echoing voices from the post-mortem room, diatribes on temperance, the Trade's vainglorious boasting on the hoardings, a medley of observation on fallen or at any rate fallible brethren and sisters, and possibly a few little items of personal experience. So as he stands in the doorway and pauses before giving his judicial nod or "no", perhaps we may harmonize the voices in his mind and reduce them to some form of order.

HOW IT IS MADE

First of all like a judge he will ask himself: "What is beer? What is stout?", and will then go on to tidy up some brute facts and figures. The main difference between ale and stout is that roasted barley and malt give flavour and colour to the stout which is made with softer water. Beer, the family name of both, is made in five stages. The first which consists of steeping the barley in water for two days and allowing it to germinate for eight is called *malting*. The starch of the barley is converted by appropriate enzymes to soluble dextrans and sugars and by an analogous process the proteins are largely converted to soluble products. The malting is ended by putting the "green malt" in a kiln and raising the temperature in three days to 200° F. (93° C.). The second stage, *mashing*, during which enzymic action continues, consists of reducing the malt to porridge and extracting the soluble products with hot water. The sweet liquor, the wort, is then *boiled* (stage three), which coagulates much of the nitrogenous stuff and destroys any remaining vitamin C: hops are added and besides giving taste provide valuable anti-septic resins. The fourth stage, *refrigeration*, brings the hopped wort to 60° F. (16° C.), when it is ready to meet the yeast. In *fermentation* there is a loss of 50 per cent. of the solid material of the wort. The carbohydrates are largely fermented to alcohol and carbon dioxide, and many of the simpler

The patient is placed in the semi-Trendelenburg position, which ensures that the abdominal contents fall away from the ring. An incision is made exposing the ring. The external oblique muscle is split and separated from the internal oblique and transversalis muscles, which are as a rule matted together. They need not be separated. The bulky cord with the sac is levered from its bed and freed from the edges of the ring. The sac is opened and its contents dealt with. The omentum is often adherent and has been the cause of the difficulty in controlling the hernia. As much of the omentum as can be conveniently drawn down is brought into view, ligated, and removed. This decreases the intra-abdominal pressure when the parts are consolidating later.

No time is spent freeing or removing the sac, which is left *in situ*. A needle threaded with silk is passed through the cord in front of the vas, near the ring, and tied off. This closes the sac. A needle mounted with the silver wire then takes a bite of the muscles to the inner side of the ring, passes through the cord and then through Poupart's ligament, and is twisted up; it then travels down the canal taking successive bites of muscles, cord, and Poupart's ligament to finish at the lower end of the canal. On drawing this tight the edges of the canal are approximated, and cord and sac are bound firmly to the muscles and ligament. The whole will become one fibrous mass. Interrupted sutures may be used if preferred. The external oblique is sewn over the line of the wire sutures with silk or nylon thread. The wound is then closed, and a sealed dressing applied, with a bandage which affords support and ensures comfort to the patient.

The operator should know exactly what he wants to do, and do it. It cannot be repeated too often that the operation can be performed efficiently in from ten to fifteen minutes.

The after-treatment is most important. Lung complications are the only risk to these elderly patients; they can be avoided with certainty if the patient does not stay in bed. He is up next day and sits in a chair. He takes it easy—that is all; if he wants to walk about he is welcome to do so. The only likely sequel is atrophy of the testis from interference with its blood supply. This is no hardship at the age at which the operation is usually performed.

The results are excellent. Many patients have said they have regained the comfort of living which they had not known for years. The procedure is to be thoroughly recommended as one which will bring untold relief to a long-suffering class of patient.

The question of vitamins in beer has been a long battle and is by no means finished. The little red book says:—

"It has been shown that alcoholic beverages are not significant sources of any of the known vitamins. Further there is now good evidence that some of the pathological conditions associated with chronic alcoholism are caused by actual deficiency of the alcoholic's diet in vitamin B complex".

In other words, beri-beri and alcoholic peripheral neuritis are sisters under the skin. That was probably written before vitamin B had become a well-defined eleven, on its way to becoming a fifteen. This is what Dr. Norris has to say about the three leading members of the team:—

"In the case of aneurine there is some loss when barley is malted, but little change in mashing and boiling. In fermentation, however, a remarkable change takes place, most of the aneurine in the wort being taken up by the yeast at the expense of the beer, which cannot therefore be regarded as a very good source of the vitamin. The amounts recorded in $\mu\text{gm.}$ per pint range from about 7 to 35, and contents as high as 85 have been found in certain strong ales. With regard to riboflavine there is an increase in malting and fermentation, many yeasts having the power of synthesizing riboflavine, with the result that the beer contains appreciable amounts and the yeast crop is greatly enriched. The riboflavine content of beers ranges from 200 to 800 $\mu\text{gm.}$ per pint, the higher limit only being attained by some strong ales".

Riboflavine, by the way, has the gift of longevity; considerable quantities have been recovered recently from a currant bun, baked for the wedding of the Prince of Wales in 1863. It would be nice to know how it has fared in some of the old audit ales.

"Nicotinic acid [continues Dr. Norris] is also present in appreciable quantity . . . Finished beers contain on an average 5 or 6 mgm. per pint". [Then he goes on to make a proviso, so typical of this subject in its lack of finality] "The three vitamins discussed above are known to have important relations to carbohydrate metabolism in that they are constituents of the enzymes concerned. It should be remembered in this context that the carbohydrates (and nitrogenous substances) in beer make their own demands on these vitamins, and only after such demands are met will the balance of the vitamin make a positive contribution to the general diet. It is difficult accurately to assess such contribution, but it is safe to suggest that . . .".

Probably our practitioner, standing in the doorway, will have already come to the conclusion that there is some vitamin B complex in beer, but, if his patient needs it, there are surer and much cheaper ways of giving it. The cost of a glass of beer is sixpence for mild ale, sevenpence for bitter, eightpence halfpenny for old, and ninepence to one-and-fourpence for the various bottled varieties. Of this, taxation accounts for 77 per cent., and a well-known firm who are certainly not shy about advertising say that their advertising costs are less than a tenth of a penny a bottle.

A BACTERIOLOGICALLY SAFE DRINK

Although the practitioner may come to the conclusion that beer is little more than well-taxed water, he will admit that from the microbiological point of view it is one of the safest of drinks; the method of manufacture, the pH of approximately 4.2, the two antiseptics, alcohol and the hop resins, all go to make it a bad medium for pathogenic bacteria. It's not like

nitrogenous materials and much of the vitamin B complex are lost to the yeast, being necessary for its growth.

THE NUTRITIONAL VALUE OF BEER

The story of brewing is therefore one of loss from the nutritive point of view. Starting with an average barley containing some 60 per cent. of starch and 10 per cent. of protein the finished beer may contain about 3 per cent. of carbohydrate, 0.2 per cent. nitrogenous material and, the purpose of this sacrifice, the sacred ordure of the yeast, alcohol, about 3 per cent. The carbohydrates consist of degradation products of starch and are digested, providing half the energy value of beer, so is the little nitrogenous material. The calorie value, half of which comes from the alcohol, ranges from 60 per half-pint for the mildest ales to 200 for the strongest beers. Mineral salts, derived from water, materials and apparatus are present in beer. London and Dublin, because of their waters, became famous for their porters and stouts—and, of course, for several other reasons—and Burton-on-Trent for its pale ales. Dr. F. W. Norris (*Nature*, April 6, 1946) says:—

“There is a very complex interplay between the various salts present during the brewing process and the nature of the salts formed in the finished beer depends upon a number of physico-chemical factors not all of which are strictly understood”. [It is nice to know that the chemist and biochemist have not robbed beer of all its mystery.] He also says: “The valuable salts of calcium are present in beer in very variable amounts according to type and conditions of brew. In a number of analyses recently examined the lowest amount appeared to be of the order of 25 mgm. calcium per pint, the highest about 270 mgm. per pint. The calcium-phosphorus ratio appeared to average unity for a wide range of beers and stouts, and this ratio may be regarded as satisfactory. On the basis of a daily requirement of 800 mgm. of calcium it will be seen that a pint of beer might provide 10 per cent. of it. At the present time it is not possible to say what proportion of calcium and phosphorus is absorbed in the body. It is known that beer contains phytic acid derived from the grain, and investigation is proceeding whereby an accurate assay of this substance may be made. The estimation of the various fractions of organic phosphorus, hexose phosphate, phytic acid, and so on, is not at present on a satisfactory basis and until accurate methods are available, it would be invidious further to discuss the phytic acid question. Phytic acid is not itself absorbed by the body and in addition it takes up a certain proportion of calcium (and iron) which is similarly lost. In the absence of quantitative data it is nevertheless reasonable to point out that not all the calcium and phosphorus in beer is necessarily absorbed”.

The mere essayist must not get involved in the great “phytic-acid question”, in which there are several erudite and earnest schools of thought. He is on safer ground in quoting Dr. Norris on the inorganics: “Of the other nutritionally important minerals copper in small amounts and manganese are known to be present”. Then he goes on to say: “Sodium chloride and potassium salts also make in this way a useful contribution to the diet of heavy workers or workers in heated atmosphere who tend to lose abnormal amounts of these salts by sweat or excretion”. In the coal ships in which I served, somewhat economically run, they used to put table salt in the firemen’s drinking water to achieve the same purpose and stop them getting cramp in hot weather.

as a legally significant amount in cases of driving accidents.

Alcohol is between sugar which should be all burnt in the body and saccharin which is all excreted, in that about one-tenth is excreted in the urine and breath—the haunting breath smell, however, comes mostly from other volatile substances—and there is also a trace in the sweat and a dash in the milk. The concentration in the urine is 1.3 times greater than in the blood, and they rise and fall in parallel. The body can derive up to a fifth of its total energy from alcohol. It is a fuel rather than a food and it must be used; in spite of some determined attempts it cannot be stored, but it can save fats and carbohydrates from being oxidized and allow more fat to be added to the body's supply. It can also save protein from being used merely as a source of energy; in short, it has the current virtues of a corresponding quantity of sugar or lard.

What then is the action of this prized excrement of *Saccharomyces*, the yeast, this alcohol, circulating as such in the blood; what effect has it on the body? We are now getting to the very kernel of our quest, the action of alcohol on the nervous system, but there are several husks to be peeled off first.

THE EFFECT ON THE BODY

Alcohol is a "tissue poison" (Price) and if the blood alcohol is kept in being for long enough the lamentable condition of chronic alcoholism occurs and no organ is spared. Braggarts talk about "holding one's liquor like a man", but those who hold most are in fact the least manly:—"Wasting of the testicles with absence or scanty production of spermatozoa is to be found in the majority of male alcoholics dying in the prime of life, while in the female, alteration of a similar character may be discovered in the ovaries". Chronic alcoholics have less resistance to bacterial diseases, influenza, tuberculosis, pneumonia, and the like. Still our man who is asking for a glass of beer is not likely to be a chronic alcoholic—that would be like an oak in a drought pining for a little dew.

In moderate doses alcohol has no effect of importance on the respiration or, except as a carminative, on the digestion. On the circulation, by relaxing the skin vessels it causes a flushing of the skin—that nice, comfortable warm feeling—there may be a slight quickening of the pulse, but the effect on the arterial blood pressure is small and indefinite. "But [says the little red book, sponsored by the M.R.C., and beginning to warm up] no scientific ground has been discovered for any claim that alcohol has practical value as a direct stimulant of the heart in cases of threatened failure of the beat". When it appears to do so it may be because (1) it is an irritant to the mucous membrane, e.g. smelling-salts and burnt feathers; (2) by its action on the nervous system it relieves the heart from the disturbing influence of pain and anxiety.

ALCOHOL AND THE BRAIN

And that, at last, brings us to the kernel—the action of alcohol on the

that dangerous drink, milk, which is considered immaculate if it has only five million spots to the c.cm.!

In naturally conditioned ales and stouts, that is to say those containing living yeast cells—the essayist's tippale contains three million per millilitre—an intruder, *Lactobacillus pastorianus*, may occasionally convert some of the residual carbohydrates into lactic acid, giving the beer a sour taste, but it is not pathogenic. This antiseptic property of beer must have saved humanity from millions of premature deaths since the time in 3000 B.C. when the Egyptians of the Fourth Dynasty brewed from barley, and from the fact that our own forbears often had no easy access to clean drinking water many of us would not be alive if for centuries ale had not been their universal drink. Trevelyan in his "English Social History" says of the Middle Ages:—

"The staple diet was bread, beer and usually meat" [and of the Golden Age of Anne] "Except in the cider counties of the West, ale had been unchallenged in former ages as the native drink of English men, women and children at every meal, and it was only beginning to feel the rivalry of strong spirits on the one hand and of tea and coffee on the other. It was still the drink of ladies. In 1705 Lady Carnarvon imputed the fact that Miss Coke was 'extremely fallen away and her voice weak and inward' to 'her having had stale beer all this summer'. Children still drank very small beer and it was in many cases better for them than the impure water which was too often the only alternative".

A generation or so later, according to Gosse, the poet Gray was considered effeminate at Cambridge because he drank tea for breakfast, whereas the rest of the University, except Horace Walpole, drank beer. Even in 1937 each inhabitant of this island on the average lowered 13.7 gallons.

All the foregoing has a certain condoning irrelevancy. If a patient wants nourishment and vitamins in safety there are much cheaper ways of prescribing them than in beer. People like beer because the alcohol gives them a pleased feeling; that also is one of the reasons why they drink tea and coffee. Almost invariably they disliked the taste when they first tried it, but this soon became associated with the pleasure and shares its popularity.

THE FATE OF ALCOHOL IN THE BODY

Our physician will remind himself of the fate of alcohol in the body. First, it is soluble in water and is absorbed without having undergone digestive change, one-fifth in the stomach, which gives it a dramatic value in extremities of inanition, one-tenth in the upper, half in the middle and the rest in the last part of the small intestine. It is absorbed more slowly if diluted, if taken with a fatty meal and, as E. Mellanby has shown, if taken in that mysterious liquid—stout. Its presence can be detected in the blood in a few minutes, the maximum concentration is reached in half to two hours, and its metabolism proceeds at a practically constant rate for any one individual (7 to 10 c.cm. of absolute alcohol an hour). The more and the more concentrated the alcohol taken and the freer its access to the stomach and intestinal walls, the higher the blood level; 0.15 per cent. corresponds to some degree of drunkenness and in one of the States of America is regarded

he really is; . . . the effects such as the increased loquacity and freer gesticulation . . . are really narcotic effects; they result from the removal of the control exercised by the higher centres, a control which enables the individual to weigh his words and acts, and renders him self-critical and solicitous as to the impression he is making on other people". [Yes, but] "The mildly narcotic action of alcohol is probably the most important from the therapeutic point of view. In many cases of illness the condition of the patient is aggravated and his recovery retarded by anxiety as to the course and outcome of his malady and by worry concerning his affairs and his family. Such anxiety may definitely impair the prospect of recovery and in so far as alcohol allays it and promotes rest it has definite therapeutic value" [and] "In promoting sleep and improving appetite alcohol performs a real service, and the relaxation of nervous tension which it produces may even contribute to the reduction of a febrile temperature". [Yea, verily, and] "The mildly narcotic action of alcohol finds its chief use in the treatment of acute infection accompanied by fever" [and further] ". . . its value in maintaining the strength during the critical period of an illness lies in the fact that it is at once a narcotic and a food. When the main object of the treatment is to control the restlessness and morbid anxiety of the patient the association of this action with even a limited food value is not without importance".

Ah, this sounds more relevant to our man's glass of beer:—

"During convalescence from an acute infection or during the course of a more chronic illness, alcoholic liquors may again have some value in improving the appetite . . . by removing the influence of anxiety and tedium associated with the patient's condition. A more pleasurable anticipation of meals has in itself a favouring influence on the action of digestive organs. The prescription of alcohol under such conditions again needs judgment and discretion . . ."

Quite, one must be careful not to start a habit in a neurotic, or to give alcohol to any case of mental disorder, head injury, and one might add, pyelitis. It is contraindicated in children and generally in tuberculosis, the toxin of which has some similarity in its action.

Tolerance is very slowly acquired and the mechanism unknown, although Winton and Bayliss say: "There is some evidence, however, that habitual drinkers can oxidize alcohol somewhat more rapidly than those not accustomed to it".

The popular use of alcohol for griping pains meets with a cold approval—"probably carminative"—and the spot of hot whisky for a cold almost gets a nod: "In that it assists the diversion of blood to the vessels of the skin, thereby relieving to some extent the congestion of internal organs and promoting a salutary perspiration, there is no reason to doubt that alcohol may be of some benefit, when used in this way". Then, as though having said too much, it damns a list of heresies: it is not a stimulant: its regular use does not give robustness—remember those testicles! It does not protect against infection, on the contrary . . . it is not a food for a healthy man.

Still, probably with reservations: "If its use in other connections were unknown it would still be a valuable item in the pharmacopœia". Yes, and this is the central point of the whole alcoholic matter, which explains its curtain, its charm and its caress—ethyl alcohol would be among the narcotics. The prisoner looks expectantly from the bed; in the judge's mind the voices are stilled, and he prepares to give judgment, well knowing that only if it is an adverse one is there a chance of its being set aside.

nervous system, an action that man has found so pleasant that he has drunk it for at least five thousand years and will probably continue to until the going down of his sun. And here the little red book gets positively John Knoxian:—

“... the main effects of alcohol that have any real significance are due to its action on the nervous system; [then, having said that its direct effect on the other systems is practically nil, it goes on] a further conclusion of capital importance which emerges is that the action of alcohol on the nervous system is essentially sedative [and with a bang] ... it is, in short, from first to last a narcotic drug; [and then, rather naggingly] ... always a lowering of functional activity”.

The mental effects it creates are “a sense of careless well-being or of bodily and mental comfort”; and the way it does it:—“Alcohol successively weakens and suspends the hierarchy of functions of the brain, and therefore of the mind, in order from above downwards; that is to say, in the inverse order of their development in the individual and in the race”, and “... it will progressively effect a similar paralysis of other nerve paths in the descending order of functional dignity and complexity; [how true!] and, thus it facilitates escape from reality and from feelings of weariness, encouraging day-dreaming, wish-fulfilment and a general regression towards the earlier and more primitive levels of childhood and infancy”.

Gay lads are often accused of drinking to ape men, but apparently men drink to become like children. Still from their cold words one doubts whether the compilers of the red book realized the attraction of child thought—coloured pictures come again and there is wonder in the world, sounds and the patterns of sound are amazingly lovely, a smell-thought can unfold a glorious adventure seen from a snug retreat, one's skin is really a most amusing fellow, and all men are brothers! After all, it is a reversion to this world that is the purpose of holiday and sleep, besides addiction. We can't be trussed and trousered pillars of the chapel all the time, not if we are intelligent enough to realize that we are but tired and tiresome lumps of tissue tottering to the grave.

The way alcohol brings about this reversion is to attack the synapses, especially those recently formed where the right of way is dubious and unworn, but even the old ones are obstructed; thus two ounces of whisky at proof lessened the speed and amplitude of the knee jerk and decreased the speed of the eye-closing reflex. All the higher centres—any action requiring skill, judgment or tact—are easily affected. Typing and memory tests show many more mistakes even under small doses of alcohol than when cold sober, although the performers themselves thought they had put up a particularly good show. This self-confidence, however, is not without merit. A speaker or a player may suffer from too much nervous inhibition and the sedative action of alcohol may have use there. Also: “Whatever may be the effect of such misleading confidence in the normal business of life it often has a real value for the sick”.

The small red oracle is sarcastic about the word “stimulant”:—

“The popular belief in the stimulant qualities of alcohol, as regards nervous and other functions, seems to be of purely subjective origin and illusory. The apparent stimulation is in the main, if not wholly, an effect of the narcotic influence of the drug, which dulls the drinker's perception of unpleasant conditions in himself and in his surroundings, and may make him feel better, more efficient and stronger than

he really is; . . . the effects such as the increased loquacity and freer gesticulation . . . are really narcotic effects; they result from the removal of the control exercised by the higher centres, a control which enables the individual to weigh his words and acts, and renders him self-critical and solicitous as to the impression he is making on other people". [Yes, but] "The mildly narcotic action of alcohol is probably the most important from the therapeutic point of view. In many cases of illness the condition of the patient is aggravated and his recovery retarded by anxiety as to the course and outcome of his malady and by worry concerning his affairs and his family. Such anxiety may definitely impair the prospect of recovery and in so far as alcohol allays it and promotes rest it has definite therapeutic value" [and] "In promoting sleep and improving appetite alcohol performs a real service, and the relaxation of nervous tension which it produces may even contribute to the reduction of a febrile temperature". [Yea, verily, and] "The mildly narcotic action of alcohol finds its chief use in the treatment of acute infection accompanied by fever" [and further] ". . . its value in maintaining the strength during the critical period of an illness lies in the fact that it is at once a narcotic and a food. When the main object of the treatment is to control the restlessness and morbid anxiety of the patient the association of this action with even a limited food value is not without importance".

Ah, this sounds more relevant to our man's glass of beer:—

"During convalescence from an acute infection or during the course of a more chronic illness, alcoholic liquors may again have some value in improving the appetite . . . by removing the influence of anxiety and tedium associated with the patient's condition. A more pleasurable anticipation of meals has in itself a favouring influence on the action of digestive organs. The prescription of alcohol under such conditions again needs judgment and discretion . . ."

Quite, one must be careful not to start a habit in a neurotic, or to give alcohol to any case of mental disorder, head injury, and one might add, pyelitis. It is contraindicated in children and generally in tuberculosis, the toxin of which has some similarity in its action.

Tolerance is very slowly acquired and the mechanism unknown, although Winton and Bayliss say: "There is some evidence, however, that habitual drinkers can oxidize alcohol somewhat more rapidly than those not accustomed to it".

The popular use of alcohol for griping pains meets with a cold approval—"probably carminative"—and the spot of hot whisky for a cold almost gets a nod: "In that it assists the diversion of blood to the vessels of the skin, thereby relieving to some extent the congestion of internal organs and promoting a salutary perspiration, there is no reason to doubt that alcohol may be of some benefit, when used in this way". Then, as though having said too much, it damns a list of heresies: it is not a stimulant: its regular use does not give robustness—remember those testicles! It does not protect against infection, on the contrary . . . it is not a food for a healthy man.

Still, probably with reservations: "If its use in other connections were unknown it would still be a valuable item in the pharmacopœia". Yes, and this is the central point of the whole alcoholic matter, which explains its curtain, its charm and its caress—ethyl alcohol would be among the narcotics. The prisoner looks expectantly from the bed; in the judge's mind the voices are stilled, and he prepares to give judgment, well knowing that only if it is an adverse one is there a chance of its being set aside.

CURRENT THERAPEUTICS

VIII.—SURGICAL ANTISEPTICS

By LAWRENCE P. GARROD, M.D., F.R.C.P.

Professor of Bacteriology, University of London; Bacteriologist, St. Bartholomew's Hospital.

A PROFOUND change has taken place during the past ten years in the attitude of the profession to antiseptics. During the first world war they were generally considered to have failed in the prevention and treatment of wound sepsis, and the conventional attitude towards them became one of scepticism. This did not result in their use being abandoned: a great variety of antiseptics, choice among which seemed to be a matter rather of whim than of reason, was still in use for many purposes, long tradition apparently sustaining a practice in which scarcely anyone seriously believed. Pungent or familiar smells and bright colours seemed to be the surest passport to popularity; so great is the force of an appeal to the senses even in highly intelligent beings. In the more difficult tasks which an antiseptic can be called upon to perform, much of the practice of this period was fruitless, either because the wrong type of agent was chosen, or because a good one was applied in such a way as to give it little chance of effect.

The change of attitude which began about ten years ago was due to the advent of the sulphonamides. The chemotherapy of a streptococcal infection is in fact antiseptics on a systemic scale, and since it had proved possible to attack bacteria by chemical means in the remotest depths of the body, it had to be admitted that they might also be attacked locally in a more accessible situation, such as a wound. That the sulphonamides themselves exert an antiseptic effect when applied locally was not in fact understood until 1939: until then the view of the German school prevailed, persistently enunciated by Domagk himself, that all true chemotherapeutic agents must act in some mysterious way involving the active cooperation of living tissue and quite incapable of demonstration *in vitro*. Recent studies of the mode of action of chemotherapeutic agents generally have shown this view to be universally false.

The new successes in overcoming bacterial, and particularly septic, infection, engendered a receptive attitude which had been absent before, and a new willingness to accept laboratory findings as a guide to clinical practice. Meanwhile the stimulus of war led to further intensive research on the problems of wound infection, and the advent of penicillin gave these studies added impetus. Certainly more has been learned in the past few years than in all the rest of this century, and it is now an appropriate time to consider how these lessons should be applied in ordinary practice.

Apart from uses outside the body altogether, such as the storage of sterile

instruments, antiseptics may be used in three principal ways. One is the disinfection of the intact normal skin. This use stands apart, because the skin is a highly resistant tissue, not easily damaged: substances can therefore be applied to it with impunity which are strongly contraindicated elsewhere. The second is the disinfection of a recent wound, possibly contaminated with pathogenic bacteria which are still in the cavity of the wound, and neither very numerous nor ensconced in the surrounding tissues. The third is the local treatment of established infection, whether in a wound or in the skin, or some other superficial site: here bacteria are very numerous and much more inaccessible. These three types of use are stated in what would appear to be an ascending order of difficulty: they are of so different a nature that different agents are likely to be required for them. Before considering the choice of these agents for each purpose it is necessary to review some of their properties.

DRAWBACKS OF THE OLDER ANTISEPTICS

For any purpose but skin disinfection most of the older antiseptics are unsuitable for one (or both) of two reasons. It is a truism that bacteria are much more easily killed in a test tube than in the body: this may be due partly to their relative inaccessibility in the body, but it may also be due to the fact that the antiseptic used is inactivated, or at least much reduced in activity, by body fluids such as blood or pus. It is also well recognized that most antiseptics are even more toxic to leucocytes and other important tissue elements than to bacteria, and may thus, at least if applied for any length of time, do more harm than good. A type of antiseptic with both of these disadvantages is mercury perchloride: the same is true of iodine. Others have only one: phenol and cresols maintain their activity well in almost any medium, but are grossly toxic: oxidizing agents and hypochlorites are relatively non-toxic, but are rapidly inactivated by the constituents of the body fluids. These substances, and others related to them, no longer enter into consideration for any use about the body except in some cases application to the skin.

MODERN ANTISEPTICS

The acridines.—It may seem scarcely appropriate to describe as modern a class of antiseptic which was introduced rather more than thirty years ago, but it is justified for two reasons: several of them have only recently been synthesized, and all have been re-studied and re-applied in surgery in more efficient ways. The circumstances of their use in the first world war were highly unfavourable, and in the inter-war period the favourite preparation of any of them, the acriflavine emulsion of the B.P.C., was so compounded as to be completely inert (Garrod, 1935). The intelligent use of the acridines derives from the work of Adrien Albert and his colleagues

(1938, 1945), who re-studied the physical and chemical properties and biological activity, not only of the previously recognized compounds but of many new ones. Much is also owed to the observation of Russell and Falconer (1940-41) that a solution of proflavine, if rendered isotonic and buffered to a pH of 6.2, is little more damaging to the exposed surface of the rabbit's brain than normal saline.

It is now recognized that of the original acridine ("flavine") compounds only proflavine is suitable for clinical use. Acriflavine (trypaflavine) is a mixture of inconstant composition, more toxic, and for the purpose of powder treatment too soluble. Of the newer compounds 2:7-diaminoacridine monohydrochloride ("diflavine") and 5-aminoacridine hydrochloride ("monacrin") are the most promising. These compounds have a high degree of activity against the pyogenic gram-positive cocci (hæmolytic streptococci in particular) and *Clostridia*. High concentrations are required to exert a bactericidal action in a short time, but on the other hand, very low concentrations will inhibit bacterial growth and exert an eventual lethal effect if enabled to act for at least some hours. The presence of serum or blood reduces their activity very little. Finally, they are the least toxic of all potent synthetic antiseptics. This aspect of their action has been the subject of controversy throughout their history. That properly prepared solutions of proflavine and the new acridines are sufficiently innocuous to leucocytes and to tissues generally is now accepted; the ground of recent controversy has been the effect on tissues of their application as powders, either alone or suitably diluted with a sulphonamide. Investigators who have found that such a procedure causes undue damage are Hawking (1943) and Russell and Falconer (1943) using undiluted powders, and Russell and Beck (1944) using a sulphonamide-proflavine mixture. On the other hand, Selbie and McIntosh (1943) found this latter mixture relatively innocuous, and Ungar and Robinson (1943) observed no necrosis when a suspension of 2:7-diaminoacridine was injected subcutaneously, although proflavine had this effect.

Capacity to prevent wound sepsis is perfectly susceptible to experimental study, and there is an immense body of evidence dating from more than twenty years ago that acridine compounds, alone among the older antiseptics, will prevent the development of infection by various gram-positive bacteria introduced into artificial wounds in mice and other animals. More recently, in the experimental prophylaxis of gas-gangrene Hawking (1941) and McIntosh and Selbie (1942) have shown that proflavine is at least as effective as sulphonamides for this purpose. Rather less clear-cut but similar findings for proflavine in the prophylaxis of streptococcal wound infections in mice are reported by Gordon *et al.* (1947).

The cationic detergents.—It is not generally known that Domagk, the discoverer of prontosil and thus the originator of sulphonamide chemotherapy, was also responsible for introducing into medicine the cationic detergents, or invert soaps. The compound of this type which he originally described was "zephyran", now known as "zephryol" in the United States.

The peculiar chemical structure and mode of action of such compounds are well described by Albert (1942) and Gledhill (1944). The most familiar of them in this country is "cetavlon" (cetyltrimethylammonium bromide, or Ctab), the properties of which are described by Barnes (1942) and Hoogerheide (1945); another is "phemeride" (Iland, 1944). These compounds greatly reduce surface tension and have a most efficient cleansing action. They are rapidly bactericidal, particularly to staphylococci, and they are also bacteriostatic in extremely low concentrations, a fact which possibly vitiates some of the findings about their supposed bactericidal effect, since traces of the substance carried over into cultures will inhibit growth of bacteria which have been "stunned" but not actually killed. Their action on bacteria is much diminished in the presence of body fluids. Application, whether to the skin or to exposed tissues, is painless and non-irritant, but there is nevertheless a toxic effect on individual cells; for instance, an 0.1 per cent. solution of cetavlon causes rapid lysis of leucocytes (Barnes, 1942).

The sulphonamides.—The introduction of sulphonamide powders into wounds for the prevention of sepsis was first practised in 1939. Experimental evidence in favour of this procedure is plentiful, but in spite of widespread clinical use, there is little clear proof of its efficacy. So far as war experience is concerned, the circumstances of the earlier campaigns were unfavourable to the collection of balanced evidence, and later in the war attention was concentrated on the effects of penicillin. The findings of Bentley and Thomson (1945) in casualties during the battle for the Gothic Line indicate that local sulphanilamide, although inferior to penicillin, materially reduces the frequency of sepsis. Sulphanilamide is actually inferior to sulphathiazole for this purpose, owing to its high solubility and thus more evanescent effect. It is difficult to appraise the significance of Meleney and Whipple's (1945) analysis of the effect of local and systemic sulphonamide treatment in over 2000 civilian cases: their conclusion is that such treatment did not diminish the frequency of infection. This is at variance both with general experience and with theoretical expectation. Sulphathiazole, either alone or as a vehicle for some more potent antiseptic, must be granted a definite place in the prophylactic treatment of wounds.

The antibiotics.—The first antibiotic to be studied in a thorough and systemic way, originally known as gramicidin and now as tyrothricin, is in fact, owing to its systemic toxicity, now used only as a local antiseptic. Penicillin and streptomycin, on the other hand, although their greatest value derives from their systemic effect, are also capable of use as antiseptics. Penicillin in particular, owing to its complete absence of toxicity, its reasonably rapid bactericidal effect, and its sustained activity in inflammatory exudates regardless of their pH and chemical and cellular content, is an ideal antiseptic for many purposes. It is not necessary to adduce evidence for this; the fact is well recognized, and indeed, perhaps the most important question with which the future of antiseptics is con-

(1938, 1945), who re-studied the physical and chemical properties and biological activity, not only of the previously recognized compounds but of many new ones. Much is also owed to the observation of Russell and Falconer (1940-41) that a solution of proflavine, if rendered isotonic and buffered to a pH of 6.2, is little more damaging to the exposed surface of the rabbit's brain than normal saline.

It is now recognized that of the original acridine ("flavine") compounds only proflavine is suitable for clinical use. Acriflavine (trypaflavine) is a mixture of inconstant composition, more toxic, and for the purpose of powder treatment too soluble. Of the newer compounds 2:7-diaminoacridine monohydrochloride ("diflavine") and 5-aminoacridine hydrochloride ("monacrin") are the most promising. These compounds have a high degree of activity against the pyogenic gram-positive cocci (haemolytic streptococci in particular) and *Clostridia*. High concentrations are required to exert a bactericidal action in a short time, but on the other hand, very low concentrations will inhibit bacterial growth and exert an eventual lethal effect if enabled to act for at least some hours. The presence of serum or blood reduces their activity very little. Finally, they are the least toxic of all potent synthetic antiseptics. This aspect of their action has been the subject of controversy throughout their history. That properly prepared solutions of proflavine and the new acridines are sufficiently innocuous to leucocytes and to tissues generally is now accepted; the ground of recent controversy has been the effect on tissues of their application as powders, either alone or suitably diluted with a sulphonamide. Investigators who have found that such a procedure causes undue damage are Hawking (1943) and Russell and Falconer (1943) using undiluted powders, and Russell and Beck (1944) using a sulphonamide-proflavine mixture. On the other hand, Selbie and McIntosh (1943) found this latter mixture relatively innocuous, and Ungar and Robinson (1943) observed no necrosis when a suspension of 2:7-diaminoacridine was injected subcutaneously, although proflavine had this effect.

Capacity to prevent wound sepsis is perfectly susceptible to experimental study, and there is an immense body of evidence dating from more than twenty years ago that acridine compounds, alone among the older antiseptics, will prevent the development of infection by various gram-positive bacteria introduced into artificial wounds in mice and other animals. More recently, in the experimental prophylaxis of gas-gangrene Hawking (1941) and McIntosh and Selbie (1942) have shown that proflavine is at least as effective as sulphonamides for this purpose. Rather less clear-cut but similar findings for proflavine in the prophylaxis of streptococcal wound infections in mice are reported by Gordon *et al.* (1947).

The cationic detergents.—It is not generally known that Domagk, the discoverer of prontosil and thus the originator of sulphonamide chemotherapy, was also responsible for introducing into medicine the cationic detergents, or invert soaps. The compound of this type which he originally described was "zephyran", now known as "zephyrol" in the United States.

static effect, and are certainly ideal for application to the surgeon's hands before donning gloves, since it has been shown that sweat contained in gloves is sterile, or apparently sterile, after two hours' wear following their application. This is of great importance from the point of view of wound contamination from glove perforations, and in this connexion it seems to be immaterial whether skin bacteria are actually killed or merely imprisoned in a film formed over the skin, as suggested by Miller *et al.* (1943). For emergency hand disinfection, or the disinfection of hands believed to be contaminated with pathological material, one of the ordinary coal tar disinfectants or dettol may be used: the last named can be used undiluted, and is said to protect the skin against re-contamination for some time.

(2) *The disinfection of a recent wound.*—Exposed tissues are much more susceptible than the skin to the toxic effects of antiseptics, and if this fact is to be given full weight, the choice for this purpose is much more restricted. Whether toxicity should be an absolute bar is, nevertheless, open to argument. If all or most of the pathogenic bacteria in a wound can be killed by an application which does a certain amount of damage to the tissue, is that not a reasonable price to pay for achieving the desired result? This doctrine finds an extreme illustration in the old practice of pressing a match dipped in pure phenol over the site of a puncture by a septic needle or scalpel point; the whole infected area is thus simply destroyed. It is, nevertheless, preferable to use some reagent which will cause the least possible degree of tissue damage consistent with antibacterial activity, and this becomes imperative if the wound is large.

What is the correct treatment of an extensive lacerated wound heavily contaminated with dirt? Probably the best reagent for preliminary treatment is a solution of a quarternary ammonium compound, such as cetavlon; this is relied on rather for its cleansing than for its antiseptic action, which is much impaired in the presence of blood. The necessary surgical treatment follows, and the most enthusiastic advocate of antiseptics must admit that his methods are only subsidiary to the surgical removal of grossly contaminated or traumatized tissue. Whether or no suture is then possible or advisable, a cavity remains in which pathogenic bacteria may still exist in small numbers. All antiseptics fit for application to a large area such as this are slow-acting, and the best way of ensuring their continued activity for some hours is to apply them in solid form, so that they pass slowly into solution. Of the *sulphonamides*, sulphathiazole has the optimum degree of solubility. The cavity should thus be dusted with sulphathiazole powder, and to this may be added either an acridine or penicillin.

If an acridine is to be used, it must be either *proflavine hemisulphate* or *5-aminoacridine hydrochloride* (aminoacrine hydrochloride B.P.): these two compounds are official in the 1948 B.P., and both form solutions of a pH of about 6.5. Proflavine sulphate forms a highly acid solution, and has been dropped from the B.P.: acriflavine remains in it, but should nevertheless not

cerned is whether or not penicillin is to replace synthetic antiseptics altogether for some purposes.

PRACTICAL ANTISEPSIS

(1) *The disinfection of the normal skin.*—It is impossible to sterilize the skin. Its "resident" flora, consisting largely of non-pathogenic staphylococci and diphtheroids, is in part deeply situated and incapable of eradication. All that is possible or necessary is to destroy the "transient" flora, bacteria which have been picked up by contact and may include pathogenic species; these, on healthy skin, are superficially situated.

There is a choice of methods for this purpose, all of which are more or less efficient, and an enormous literature on their relative merits. Much depends upon circumstances—whether the skin is that of patient or surgeon, whether disinfection precedes a mere puncture or an extensive operation, and how much time is to be allowed for the process. The last factor is important and often overlooked; it is, for instance, theoretically absurd to use a slow-acting antiseptic, such as an acridine or mercurial salt or compound, when its effect is expected to be achieved in perhaps less than a minute. If such reagents are to be used for the preoperative preparation of the skin, this should precede the operation by an hour or more.

It has been shown experimentally by Colebrook, and confirmed recently by Gardner (1946) that *iodine*, in the form of a 2 per cent. solution in 70 per cent. alcohol, is a most efficient and rapidly acting skin disinfectant. Its drawback as a prelude to major operations is its damaging effect on tissues which may be contaminated with it by contact with the wound edge; this is particularly true of laparotomy, when inflammatory changes induced by iodine in the peritoneum have been said to be capable of resulting in subsequent adhesions.

Alcohol has many advocates, including in recent times Neufeld (1943; and co-workers, 1941), Sobernheim (1943) and Pohle and Stuart (1940): it is undoubtedly capable of killing at least the great majority of pathogenic bacteria on the skin in a very short time, and is superior to ether. Its optimum concentration is 75 per cent. by volume, but since the skin is often moist, it usually acts well when applied undiluted; Archer (1945) suggests 80 per cent. as probably the best average concentration for use on the skin.

Almost in an opposite camp to the advocates of alcohol are the protagonists of the *quarternary ammonium compounds*: zephyran (Shumacker and Bethea, 1943; Lovell, 1946), ceepryn (Kramer and Sedwitz, 1944; Helmsworth and Hoxworth, 1945), phemerol (Brown, *et al.*, 1944), and cetavlon (Williams, *et al.*, 1944). Gardner (1946) found zephyran superior to cetavlon in the type of test he used. These substances have a marked cleansing action, and might well on that account be used as a preliminary to some other form of treatment, such as the application of spirit. They have a marked bacterio-

and sulphathiazole a diluent, although it has an action *per se*. To this should be added only one other agent, whether penicillin or an acridine. To complicate treatment by introducing other antiseptics is to run the risk of incompatibilities, and to confuse the interpretation of results; it is also likely to increase toxic effects without any commensurate gain in antibacterial action.

(3) *The treatment of established infections.*—Chronic suppuration is not the problem that it was, but it still exists. Its efficient treatment depends first upon ascertaining the nature of the infection. The sulphonamides are relatively inactive in pus, and only the most sensitive bacteria can be attacked by them; these are hæmolytic streptococci, which can often be eliminated from superficial infected wounds by local sulphonamide treatment (Colebrook and Francis, 1941). For other infections more vigorous measures are required. Here again the choice usually lies between the acridines and penicillin. Granulation tissue bathed in pus is far more resistant than normal tissues to the toxic action of the acridines, and it was first shown by Mitchell and Buttle (1942, 1943) that proflavine or diflavine (2:7-diaminoacridine) can be introduced into suppurating wounds, undiluted in powder form in quantities up to 0.5 gm., without ill-effect and with remarkable results in controlling sepsis. The secret of success here is again the prolonged effect ensured by the slow solution of the not too soluble powder. Other advocates of the acridines in the treatment of sepsis are Poate (1944a and b), Rank (1944), and Heggie, Warnock and Nevin (1945). These authors, as others quoted earlier, were writing in the dawn of the penicillin era, and Rank probably assessed the new position correctly when he wrote: "It seems to me that what can be done with other antiseptics can be done with penicillin appropriately used, more often, sooner and with more uniformly good results".

Gram-negative infection, due to *Ps. pyocyanea*, *Proteus* and coliform bacilli generally, presents a special problem; the acridines have much less effect on it and penicillin in most cases none. Tyrothricin, reported on favourably by Kozoll *et al.* (1946) for treating streptococcal and staphylococcal infections, is also useless. Undoubtedly the best antiseptic for this type of infection is a solution of *streptomycin*; applied by spray or as a wet dressing it will often sterilize an accessible wound overnight. Unfortunately, streptomycin is not yet generally available for such purposes. Other antiseptics which have been found active against gram-negative infection are phenoxetol and urea or urethane combined with a sulphonamide: clinical experience of them so far seems to have been inadequate to assess their true value.

CONCLUSIONS

Of the three principal *in vivo* uses of antisepsis, skin disinfection is a problem apart, and the prevention or treatment of wound infection is another. For the second purpose, sulphonamides have a definite but limited usefulness;

be used. The usual proportion is 1 part of the acridine to 99 parts of sulphathiazole: "thiazamide" is such a mixture containing 5-aminoacridine hydrochloride. "Flavazole", favourably reported on by McIntosh *et al.* (1945) is a chemical compound of sulphathiazole and proflavine base, two parts of which are added to 98 parts of sulphathiazole. The theoretical and experimental evidence in favour of this treatment has already been given: clinical confirmation of its value will be found in the papers of Ascroft (1944), Feggetter (1944), McIntosh and Selbie (1944), and Raven (1944). It is of some interest that all these studies were made shortly before penicillin became available. But for this new development, the acridines would finally have taken their rightful place in general estimation as the most efficient synthetic antiseptics for primary wound treatment.

A deep penetrating wound such as that produced by a high velocity missile cannot be treated in this way. Such wounds are uncommon in civilian practice. In this or any type of wound incapable of efficient local treatment, the prevention of infection must depend upon systemic chemotherapy. A special case is the small puncture wound known to be dangerously infected, such as that produced by an instrument in use for a septic case.

I suggested many years ago (Garrod, 1931) by analogy with mouse experiments, that the rational treatment for this would be infiltration of the area with a solution of an acridine. This technique has since been successfully employed by Arden (1945), using a 0.1 per cent. solution of 5-aminoacridine hydrochloride, of which as much as 30 c.cm. was injected into the tissues bordering wounds without ill-effect.

The alternative to an acridine is *penicillin*, which should be added as the calcium salt to sulphathiazole so that 1 gm. of powder contains 5000 units of penicillin. The same preparation can be used as a snuff for the treatment of nasal and nasopharyngeal infections and carrier states, when the organism is a staphylococcus, streptococcus, diphtheria bacillus or meningococcus. Penicillin is more potent than the acridines and entirely free from toxicity; on the other hand it is much more soluble and quickly absorbed and must therefore have a more evanescent effect. The studies of Florey and Cairns in North Africa in 1943 made it clear that such a powder has a remarkable effect in controlling wound sepsis, but the adoption of the systemic route of administration as supplies of penicillin increased interrupted further studies on these lines. I am aware of no further information by which the value of penicillin-sulphonamide powder can be assessed. This is perhaps the place to point out that the casualty department of any hospital, and even the surgery of the individual practitioner, offer opportunities for research on this subject. It is a truism that no two wounds are alike, but if two forms of treatment are used in alternate cases for a year or more this objection begins to lose its force, and some evidence of the relative efficiency of the two methods ought to be obtainable.

I believe it to be a mistake to use more than one potent antiseptic in any single case. In the procedure suggested cetavlon is chiefly a cleansing agent

REVISION CORNER

HYPERHIDROSIS

EXCESSIVE local sweating is relatively common and is important, partly because of the inconvenience caused by the moisture itself and partly by reason of other conditions to which it may lead. There are certain general diseases which can be responsible, such as thyrotoxicosis, rickets, obesity, and chronic toxic conditions, such as alcoholism. But sweating with fear, apprehension or excitement is more common, and in practice emotional stress or tension plays a far more important part. An overactive sweating reflex can be made permanently worse by certain local conditions, such as flat feet, and temporarily so by prolonged standing, overwalking, overworking, and by the drinking of hot fluids such as hot tea and hot soups. All these are more likely to be effective in hot weather. The parts most usually involved and for which advice is sought are the hands, feet and axillæ, the latter especially in women, when the clothes are often stained or even in time destroyed. The palms and soles are affected almost equally in the sexes.

The sweat alone may dissolve out irritant dyes and other chemicals from clothing, e.g. paraphenylene-diamine from dark brown dyes, or chrome products from the leather of shoes, wrist-watch straps or hatbands, which irritate the skin and set up contact dermatitis in the areas so exposed. But the frequent or constant presence of moisture may also encourage the growth of micro-organisms. In the axillæ and on the feet the sweat and sebum may be attacked by these and broken down into organic acids and other products offensive to the nose and destructive to the clothing. On the feet, especially in the toe clefts, pathogenic fungi such as the epidermophyton may find a foothold and produce the characteristic sodden appearance of "toe-rot" common in young people; whilst on the hands, monilia may flourish and give rise in the nail-folds to paronychia, and on the webs to *erosio interdigitale blastomycetica*; or the virus of infective warts may start a crop of these disfiguring lesions. Warts are undoubtedly more common and more numerous in hyperhidrotic subjects, both on the hands and on the soles of the feet (plantar warts). Even septic organisms may find an entry into the inflamed, macerated and cracked skin of the toes and occasionally cause acute lymphangitis in the foot. In the groins excessive sweating also favours the growth of fungi, commonly the epidermophyton, causing the scaly erythema called Dhobie's itch (*tinea cruris*).

TREATMENT

The radical cure of excessive local sweating is a matter of some difficulty and there is unfortunately no effective measure which can guarantee permanent freedom. But in most cases much can be done to restore the part to a more normal condition. It is unlikely, for instance, that anyone who is subject to moist hands just before an examination or an interview, or an appearance in public, can be completely relieved of his disability even by a prolonged course of psychotherapy: but at least the affected area of skin can be helped out by local hygiene. Hygiene is particularly important in preventing some of the grosser complications; and care of the feet by simple cleansing, frequent changing of socks and footwear, and the wearing of open shoes or sandals in hot weather will do much to alleviate the worst features. The wearing of sandals should no longer be stigmatized as a mark of the æsthete or crank, but should be prescribed as a routine for the hyperhidrotic subject. Flat feet should receive the attention of the orthopædist, and light clothing and avoidance of over-clothing should be encouraged. By the same token, dress preservers for women's armpits often cause more trouble than they relieve.

Such *drugs* as are available have proved disappointing in most dermatologists' hands: but a surgeon of my acquaintance can get through a morning's operating in

their action can be reinforced either by one of the acridines, which are the most efficient of the synthetic antiseptics, or by penicillin or other antibiotics. The indications for choice between these two alternatives have yet to be clearly defined.

References

- Albert, A. (1942): *Lancet*, **ii**, 633.
 —, Francis, A. E., Garrod, L. P., and Linnell, W. H. (1938): *Brit. J. exp. Path.*, **19**, 41.
 —, Rubbo, S. D., Goldacre, R. J., Davey, M. E., and Stone, J. D. (1945): *Ibid.*, **26**, 160.
 Archer, G. T. L. (1945): *Brit. med. J.*, **ii**, 148.
 Arden, F. (1945): *Med. J. Austral.*, **32**, 486.
 Ascroft, P. B. (1944): *Lancet*, **i**, 594.
 Barnes, J. M. (1942): *Ibid.*, **i**, 531.
 Bentley, F. W., and Thomson, S. (1945): *Brit. med. J.*, **i**, 471.
 Brown, W. E., Gunderson, M. F., Schwartz, P., and Wilder, V. M. (1944): *Surg. Gynec. Obstet.*, **78**, 173.
 Colebrook, L., and Francis, A. E. (1941): *Lancet*, **i**, 271.
 Feggetter, G. Y. (1944): *Ibid.*, **i**, 593.
 Gardner, A. D. (1946): *Ibid.*, **i**, 683.
 Garrod, L. P. (1931): *St. Bart's Hosp. Rep.*, **64**, 85.
 — (1935): *Pharm. J.*, **80**, 323.
 Gledhill, W. S. (1944): *Austral. J. Sci.*, **6**, 170.
 Gordon, J., et al. (1947): *J. Hyg.*, **45**, 297.
 Hawking, F. (1941): *Brit. med. J.*, **i**, 263.
 — (1943): *Lancet*, **i**, 710.
 Heggie, J. F., Warnock, G. B. R., and Nevin, R. W. (1945): *Brit. med. J.*, **i**, 437.
 Helmsworth, J. A., and Hoxworth, P. I. (1945): *Surg. Gynec. Obstet.*, **80**, 473.
 Hoogerheide, J. C. (1945): *J. Bact.*, **49**, 277.
 Iland, C. N. (1944): *Lancet*, **i**, 49.
 Kozoll, D. K., Meyer, K. A., Hoffman, W. S. and Levine, S. (1946): *Surg. Gynec. Obstet.*, **83**, 323.
 Kramer, G. B., and Sedwitz, S. H. (1944): *Amer. J. Surg.*, **63**, 240.
 Lovell, D. L. (1946): *Archiv. Surg.*, **53**, 304.
 McIntosh, J., and Selbie, F. R. (1942): *Lancet*, **ii**, 750.
 — (1944): *Ibid.*, **i**, 591.
 —, Robinson, R. H. M., and Selbie, F. R. (1945): *Ibid.*, **ii**, 97.
 Meleney, F. L., and Whipple, A. O. (1945): *Surg. Gynec. Obstet.*, **80**, 263.
 Miller, B. F., Abrams, R., Huber, D. A., and Klein, M. (1943): *Proc. Soc. exp. Biol. N.Y.*, **54**, 174.
 Mitchell, G. A. G., and Buttle, G. A. H. (1942): *Lancet*, **ii**, 416.
 —, — (1943): *Ibid.*, **ii**, 287.
 Neufeld, F. (1943): *Z. Hyg. Infektr.*, **125**, 287.
 — and Schiemann, O. (1941): *Ibid.*, **124**, 751.
 —, and Schutz, O. (1941) *Ibid.*, **123**, 396.
 Poate, H. R. G. (1944a): *Lancet*, **ii**, 238.
 — (1944b): *Med. J. Austral.*, **31**, 242.
 Pohle, W. D., and Stuart, L. S. (1940): *J. infect. Dis.*, **67**, 275.
 Rank, B. K. (1944): *Med. J. Austral.*, **31**, 629.
 Raven, R. W. (1944): *Lancet*, **ii**, 73.
 Russell, D. S., and Beck, D. J. K. (1944): *Brit. med. J.*, **i**, 112.
 —, and Falconer, M. A. (1940-41): *Brit. J. Surg.*, **28**, 472.
 —, — (1943): *Lancet*, **i**, 580.
 Selbie, F. R., and McIntosh, J. (1943): *J. Path. Bact.*, **55**, 477.
 Shumacker, H. B., Jun., and Bethea, W. R., Jun. (1943): *Surgery*, **14**, 931.
 Sobernheim, G. (1943): *Schweiz. med. Wschr.*, **73**, 1280, 1304, 1333.
 Ungar, J., and Robinson, F. A. (1943): *Lancet*, **ii**, 285.
 Williams, R. E. O., et al. (1944): *Ibid.*, **i**, 787.

A severe *ulcerative stomatitis* or necrotic stomatitis may of course occur as a complication of certain blood diseases, particularly agranulocytosis and leukæmia. The development of ulcerative gingivitis in a patient under treatment with thicuracil should be regarded as a definite indication for stopping the drug immediately and checking the white cell and differential counts. In leukæmia the splenic and hepatic enlargement and the involvement of various groups of glands will usually indicate the cause, but in doubtful cases the white blood cell count and differential count will help to establish the diagnosis. *Infective mononucleosis* should be considered as a differential diagnosis in cases of acute ulcerative tonsillitis associated with generalized glandular enlargement and fever in an adolescent or young adult.

Occasionally, oral infection may occur as a result of malnutrition, particularly if there is vitamin C deficiency causing hæmorrhage into the gums; sometimes it occurs as a sequel of acute infection in children, particularly after severe measles or diphtheria. *Thrush* may cause halitosis in young infants, and sometimes in older children, but it is a condition which is readily identified by the white patches on the gums, cheeks and tongue, and can be confirmed by examination of a smear from the lesion.

In adults, halitosis is often due to *postnasal infection*. This should be suspected if clinical examination reveals a congested granular pharynx with a dry mucous membrane, and evidence of sinus infection may be afforded by a streak of muco-pus running down from the posterior nares. Confirmation of sinus infection may be obtained by transillumination or X-ray examination. *Infection involving the lower respiratory tract* may also cause halitosis, and of this group chronic bronchitis is the most common. Bronchiectasis should be suspected if persistent cough with mucopurulent sputum develops after pneumonia; if the history is one of copious and offensive sputum occurring suddenly during convalescence from pneumonia, then lung abscess is the most likely cause, though in either case X-ray examination will be essential to establish the diagnosis.

Gastric stasis may often cause halitosis, and is a frequent cause of foul breath in young children as well as in adults. This cause should be suspected if this presenting symptom is associated with a history of dyspepsia, loss of appetite and flatulence. Halitosis in these cases is most noticeable first thing in the morning, and if flatulence occurs the eructations have a particularly offensive smell. The breath is not offensive in peptic ulcer patients except in old-standing cases when there is pyloric obstruction.

DISTINCTIVE ODOURS

Occasionally the breath has a peculiarly characteristic odour; the sweet and rather sickly smell of acetone is easy to identify, but does not, of course, necessarily mean that the patient is a diabetic; it is merely an indication of abnormal carbohydrate and fat metabolism and occurs during starvation, and with acute febrile infections, particularly those in which vomiting is a distinctive feature. Another distinctive odour that is often detected in the breath is the peculiar stale uriniferous odour associated with uræmia and renal failure.

Extraneous causes of foul breath are for the most part readily identified; excessive smoking gives a characteristic "stale tobacco" smell to the breath, and is more common in pipe smokers, particularly those who neglect to clean their pipes. Onions, garlic and certain other vegetables, and herbs used for flavouring, are similarly readily identified, although the smell of "stale alcohol" in the breath is now becoming as rare as the chronic alcoholic!

CONCLUSION

In spite of careful examination and investigation, in a few cases it will prove almost impossible to establish the actual cause of halitosis. In these few cases, the rare neurogenic and congenital causes should be considered; of the former cardiospasm

comfort if he has first applied "odorono" (sodium hexa-metaphosphate) to his overheated brow, and this saves considerable man- or woman-power, by dispensing with the gentle ministrations of the nurse usually detailed for that purpose. Such astringents as 5 per cent. formalin mopped on to the soles of the feet daily may help to shut down sweating for a time. Bland powders such as boracic, talc, or talc and salicylic acid will absorb sweat and offer a large evaporating surface which tends to keep the parts cool and dry.

X-rays have long been found of value in the treatment of local sweating but occasionally they fail; perhaps, as might be expected, more particularly in those cases in which the emotional factors are paramount. Anyhow, large doses should be avoided and treatment should be in the hands of an expert.

The physician who sets out to treat hyperhidrosis must, as always, treat the patient. He must look for errors in general health, faulty habits, overwork, inadequate sleep, lack of holidays, and emotional strains and stresses, and, in so far as he can, correct them; for local measures applied without attention to the general condition are apt to fail in their purpose.

C. H. WHITTLE, M.D., F.R.C.P.

HALITOSIS

In spite of enterprising advertisements in the lay press, halitosis is a complaint for which relatively few patients seek medical advice. Halitosis is, however, often apparent during the course of clinical examination, and is all too often disregarded. It is an unpleasant symptom, not only for the patient but also for his immediate family contacts and friends, and a little time devoted to ascertaining the cause and in arranging suitable treatment is time well spent.

CAUSAL FACTORS

The most common cause of foul breath is, of course, *periodontal infection*. This usually develops as a result of neglecting dental hygiene; food stagnates in the gum margins, and as a result of bacterial action the attachment of the mucoperiosteum to the tooth is destroyed, so that a pocket is formed in which pus collects. Once the condition has progressed to this stage of pus formation, it is readily recognizable as a frank pyorrhœa alveolaris, with inflamed bleeding gum margins from which pus exudes, or can be expressed on gentle pressure. Occasionally, pyorrhœa may be secondary to severe dental caries which has involved the pulp cavity and progressed to form an alveolar abscess. The treatment of pyorrhœa is best left to an experienced dental surgeon; surprisingly good results are achieved by conservative methods.

Another local infective condition which causes foul breath is *Vincent's angina* or "trench mouth". This is characteristically an acute infection, accompanied by some degree of constitutional reaction—malaise and rise of temperature. The infection often starts on the tonsils or fauces and spreads forward into the mouth to involve the gum margins; the early lesions are covered with a dirty greyish membrane, which if separated leaves a raw, shallow ulcer. The gums are inflamed, swollen and tender, and superficial ulceration occurs near the line of the teeth. As the condition tends to occur in epidemics, particularly in institutions, the diagnosis of an acute case seldom presents any difficulty. In subacute and chronic cases the diagnosis may be established by swabbing the lesions, and examining the smear for Vincent's spirillum and the associated fusiform bacilli. The condition responds to local treatment with arsenic (either neoarsphenamine, 20 grains to 1 ounce (1.3 gm. to 28.4 c.cm.) or arsenical solution and glycerin in equal portions). If the infection is severe, penicillin may be given both parenterally and locally in the form of lozenges, which are allowed to dissolve slowly in the mouth.

ache is the sole complaint, it may be necessary to invoke the aid of an ophthalmologist to exclude refractive errors and a radiologist to exclude sinus infection as causes of the symptoms. A normal erythrocyte sedimentation rate is sometimes of help in reaching a decision.

MIGRAINE

Most headaches which are not psychological in origin are due to either migraine, refractive errors or sinus infection. In no condition is history-taking of greater importance than in migraine. The aura, sometimes hemianopia or the fortification spectrum, lasting as a rule about half an hour and followed by frontal headache which is often unilateral and accompanied by vomiting, the onset at puberty, and the completely normal health between attacks leave no doubt about the diagnosis. A family history of sick headaches, a tendency for attacks to coincide with menstruation, and an allergic family history are common. When the aura consists of an aphasia or hemiplegia, Jacksonian epilepsy may be thought of, and when the aura and vomiting are absent, and the headache lasts longer than the usual period of hours, other causes may have to be considered. If the patient is seen between attacks, physical examination reveals no abnormality, but during an attack the temporal artery may be abnormally prominent and tender, whilst the relief of headache produced by carotid artery compression or the administration of ergotamine tartrate may be of help in diagnosis.

It is important to differentiate the rather rare condition known as *migrainous neuralgia*. This consists of paroxysms of pain lasting for some minutes or hours, usually in the area supplied by the second division of the trigeminal nerve. It is not preceded by an aura, nor is it accompanied by vomiting.

OTHER FACTORS

Errors of refraction are a common cause of headache. Myopes are never so afflicted but in those suffering from uncorrected hypermetropia or astigmatism, frontal headache at the end of the day is common, particularly if there has been much reading or close work, and it is often accompanied by a feeling of grittiness in the eyes and some conjunctival injection. Such symptoms are readily relieved by the wearing of proper spectacles. It must be added, however, that the subjects of refractive error are also prone to experience the tension headaches due to sustained contraction of the muscles of the scalp and neck, and also that neurotic headaches may occasionally be relieved by spectacles in suggestible patients even when no appreciable refractive error is present.

When headache is due to *sinus infection* the symptoms will usually date from a head cold and be accompanied by some nasal discharge and obstruction. In frontal sinus infection the pain is felt in the area of the infected sinus and comes on about noon, passing off in the early evening. There is usually some tenderness over the affected sinus. In infection of the maxillary antrum the pain may be felt in the cheek. Whichever sinus is affected, coughing and stooping oftentimes produce an aggravation of the pain and give it a throbbing character. The pain is mitigated or removed by aspirin. Transillumination and radiological study will confirm the diagnosis, although in acute cases the abnormalities revealed may not be gross.

Hypertension, whether it be essential, renal or due to any of the rarer causes, is often accompanied by headache which is thought to be due to dilatation of the intracranial arteries. Physical examination readily reveals the cause of the headache, but it must be mentioned that in many subjects of benign hypertension the headache of which they complain is psychological in origin and unrelated to their increased blood pressure. When papilloedema is present abnormal urinary findings and blood chemistry will serve to separate the renal group, whilst the size of the heart and sphygmomanometric examination will distinguish the malignant hypertensive from those with space-occupying lesions in the skull.

is not infrequently accompanied by halitosis and may be suspected from the history of food appearing to "stick" after swallowing. Congenital defects must indeed be rare causes, but pharyngeal pouches and œsophageal diverticula are relatively easily identified by modern radiological technique. Finally, there remains a small group of cases in which halitosis has no apparent cause: unfortunate people who have always had a slightly offensive breath and who, like the man who ate the "potomak", must learn to live with their halitosis.

R. GWYN EVANS, M.B.E., M.D., M.R.C.P.

DIFFERENTIAL DIAGNOSIS OF HEADACHE

HEADACHE is one of the most common presenting symptoms in those seeking medical advice. Knowledge of the mechanism by which it is produced has been greatly increased by the work of Wolff in America and Pickering in this country. By observation of neurosurgical patients undergoing operation under local anæsthesia and by other investigatory procedures they have shown that the brain itself, the pia-arachnoid, and the bony skull are insensitive to pain, whereas, on the other hand, the intracranial and pericranial arteries and the cerebral venous sinuses together with the dura mater, particularly that part of it adjacent to blood vessels, are sensitive to pain. Most headaches of intracranial origin arise from dilatation of intracranial arteries or by traction upon them or other pain-sensitive structures. Disturbances of this nature above the tentorium produce pain which is transmitted through the trigeminal nerve and felt anterior to a line joining the two ears, whilst similar processes below the tentorium produce pain which is transmitted through the ninth and tenth cranial nerves and the upper three cervical nerves, and is felt posterior to this line.

The belief that increased intracranial tension *per se* is a cause of headache has been discarded and it is now clear that the headache associated with space-occupying lesions in the skull is produced by traction on the dura mater, venous sinuses or intracranial arteries. Reduction of intracranial pressure may, however, cause headache due to the dilatation of intracranial arteries which results from it. Other workers have shown that many headaches of extracranial origin, such as neurotic headaches and headaches due to refractive errors, are often due to prolonged spasm of the muscles of the scalp and neck.

PSYCHOGENIC FACTORS

In the majority of patients in whom headache is the clamant symptom the cause of their disability is *emotional instability* and not organic disease, the common psychological processes responsible being hysteria and anxiety. In the hysterical group diagnosis hardly ever presents any difficulty. The patient, invariably a woman, describes the headache in terms which purport to imply that she is suffering tortures greater than anyone has ever before experienced, and her pain never remits and never responds to any remedy which may be prescribed. Despite this she presents the appearance of robust physical health, and the history, the background and temperament of the patient, combined with a completely negative physical examination, preclude the necessity for ancillary investigation as to the cause of her symptoms. The diagnosis is usually as easy as the cure is difficult.

When *anxiety* is the process underlying headache there will usually be other symptoms, such as dizziness, tiredness, insomnia, and palpitation, and long before the end of the consultation the experienced clinician will have sensed that he is dealing with an anxiety state. The headache is usually intermittent and may last for periods of hours or days. Physical examination is essentially negative but it may reveal some tenderness in the muscles on the posterior aspect of the neck, and the pain is commonly maximal in this area. In most cases the fact that anxiety is the cause of the headache will be obvious, but in a few, and especially when head-

ache is the sole complaint, it may be necessary to invoke the aid of an ophthalmologist to exclude refractive errors and a radiologist to exclude sinus infection as causes of the symptoms. A normal erythrocyte sedimentation rate is sometimes of help in reaching a decision.

MIGRAINE

Most headaches which are not psychological in origin are due to either migraine, refractive errors or sinus infection. In no condition is history-taking of greater importance than in migraine. The aura, sometimes hemianopia or the fortification spectrum, lasting as a rule about half an hour and followed by frontal headache which is often unilateral and accompanied by vomiting, the onset at puberty, and the completely normal health between attacks leave no doubt about the diagnosis. A family history of sick headaches, a tendency for attacks to coincide with menstruation, and an allergic family history are common. When the aura consists of an aphasia or hemiplegia, Jacksonian epilepsy may be thought of, and when the aura and vomiting are absent, and the headache lasts longer than the usual period of hours, other causes may have to be considered. If the patient is seen between attacks, physical examination reveals no abnormality, but during an attack the temporal artery may be abnormally prominent and tender, whilst the relief of headache produced by carotid artery compression or the administration of ergotamine tartrate may be of help in diagnosis.

It is important to differentiate the rather rare condition known as *migrainous neuralgia*. This consists of paroxysms of pain lasting for some minutes or hours, usually in the area supplied by the second division of the trigeminal nerve. It is not preceded by an aura, nor is it accompanied by vomiting.

OTHER FACTORS

Errors of refraction are a common cause of headache. Myopes are never so afflicted but in those suffering from uncorrected hypermetropia or astigmatism, frontal headache at the end of the day is common, particularly if there has been much reading or close work, and it is often accompanied by a feeling of grittiness in the eyes and some conjunctival injection. Such symptoms are readily relieved by the wearing of proper spectacles. It must be added, however, that the subjects of refractive error are also prone to experience the tension headaches due to sustained contraction of the muscles of the scalp and neck, and also that neurotic headaches may occasionally be relieved by spectacles in suggestible patients even when no appreciable refractive error is present.

When headache is due to *sinus infection* the symptoms will usually date from a head cold and be accompanied by some nasal discharge and obstruction. In frontal sinus infection the pain is felt in the area of the infected sinus and comes on about noon, passing off in the early evening. There is usually some tenderness over the affected sinus. In infection of the maxillary antrum the pain may be felt in the cheek. Whichever sinus is affected, coughing and stooping oftentimes produce an aggravation of the pain and give it a throbbing character. The pain is mitigated or removed by aspirin. Transillumination and radiological study will confirm the diagnosis, although in acute cases the abnormalities revealed may not be gross.

Hypertension, whether it be essential, renal or due to any of the rarer causes, is often accompanied by headache which is thought to be due to dilatation of the intracranial arteries. Physical examination readily reveals the cause of the headache, but it must be mentioned that in many subjects of benign hypertension the headache of which they complain is psychological in origin and unrelated to their increased blood pressure. When papilloedema is present abnormal urinary findings and blood chemistry will serve to separate the renal group, whilst the size of the heart and sphygmomanometric examination will distinguish the malignant hypertensive from those with space-occupying lesions in the skull.

Of the *space-occupying lesions* tumour is the most common cause of headache, which is usually intermittent and tends to occur in the early mornings and to be provoked by physical exertion. It is often unilateral, and in such cases if papilloedema is absent its site is of definite localizing value. When papilloedema or neurological signs are present diagnosis is not difficult, but in the absence of these signs radiological examination of the skull may prove the diagnosis. Ventriculography or arteriography may be necessary for accurate localization or even to make certain that a tumour is definitely present. In subdural hæmatoma the history of injury, and in abscess the presence of aural or pulmonary suppuration, will suggest the diagnosis.

Post-traumatic headaches may be due to psychological factors but a proportion are due to adhesions between the dura and arachnoid causing traction on the former, in which case they tend to be localized to the site of the injury.

A. G. W. WHITFIELD, M.B., M.R.C.P.

(The treatment of headache will be dealt with in a subsequent article.)

NOTES AND QUERIES

Heredity and Leukæmia

QUERY.—A patient of mine, aged three-and-a-half years, has died from acute lymphatic leukæmia. A brother, also aged three-and-a-half years, and a first cousin aged six years, died from this complaint some years ago. Is leukæmia a familial disease? Is there a likelihood that other members of these two families will be leukæmic? What is the present position regarding prophylaxis and treatment?

REPLY.—By inbreeding mice it is possible to develop strains of which 90 per cent. develop leukæmia. In other pure strains the incidence is less than 2 per cent. In the strains with a 90 per cent. incidence of leukæmia, it appears that the unaffected 10 per cent. carry the morbid trait, for their progeny have an equally high incidence of leukæmia. Thus in pure-bred mice, leukæmia appears to depend upon an intrinsic genetic factor, although external factors play a part in deciding whether or not the disease becomes manifest. In man we do not deal with pure strains and the hereditary factor in leukæmia is less evident, but nevertheless it exists.

Videback (1947) studied the pedigrees of 209 patients with leukæmia and 200 controls. He obtained evidence of leukæmia in 17 of the 4,041 relatives of the patients with leukæmia and in only 1 of the 3,641 relatives of the controls. Adding his own cases of familial leukæmia to those in the literature he collected in all 39 families: in 33 of the families there were only two cases of the disease, in 4 three, in 2 four.

In brief then, leukæmia is more likely to occur in the relatives of a leukæmic patient than in the general population. Nevertheless, it is a rare disease and the risk is relatively small. The possibility that other members of the present family will have leukæmia cannot be excluded, but the odds are against it. No method of

prophylaxis is known. Treatment is by X-rays or chemotherapeutic agents, which were the subject of an article in the June number of *The Practitioner* (Mitchell, 1948).

References

- Videback, A. (1947): "Heredity in Human Leukæmia," Copenhagen.
 Mitchell, J. S. (1948): *The Practitioner*, 160, 476.
 PROFESSOR L. J. WITTS, M.D., F.R.C.P.

The Genes and Sex Determination

QUERY.—It is of common occurrence to find families in which there is a long series of children of the one sex; does this indicate a peculiarity of the gene in either parent or is the incidence no greater than would be anticipated in any large series? Has any progress been made recently in foretelling the sex of pregnancies?

REPLY.—It is now generally accepted that in our species sex is determined by genes which in their action are uninfluenced by environmental forces. There are male-determining and female-determining genes. The former have, through time, become concentrated in the autosomes and in the Y-chromosome, the latter in the X-chromosome. The sex chromosomes (the X and Y) therefore act as differentials. Sex is determined by the quantitative relationship of the male and female-determining genes. In the male (2 sets of autosomes, 1 X and 1 Y) this relationship $M > F$ results in a male. In the female (2 sets of autosomes, 2 Xs) $M < F$ in a female.

The human male is heterogametic, producing X-chromosome and Y-chromosome bearing spermatozoa. All ova contain one X. Conception involves the construction of an XX or of an XY individual, a female or a male. If the X and the Y spermatozoa are produced in equal numbers, are equally capable of fertilizing the ovum, and

if the XY and XX zygotes are equally viable, then the primary sex-ratio, that which obtains among the newly conceived, will be equality as will also the secondary, that among the newly born.

The facts that the secondary sex-ratio among stillbirths tends to be higher than this, that the sex-ratio among abortions would seem to be still higher, and that after birth in all age-groups a sexually selective mortality removes more males than females, suggest that the primary sex-ratio is far removed from equality, far more males than females being conceived. This is not proven, but it does seem reasonable to entertain the view that the sexually selective mortality which operates after birth does so also during intra-uterine life. It is not known whether more Y-bearing than X-bearing sperm are produced or whether the Y is more efficient in fertilization. Disregarding this last point, it is a matter of chance whether the ovum is fertilized by an X- or by a Y-bearing spermatozoon. This being so it follows that in certain families there will be none but boys, in others none but girls. Experiments with rats many years ago gave results which seemed to show quite clearly that it was possible by continued selection to obtain high sex-ratio and low sex-ratio strains. Maybe this difference was associated with significant differences in the physical or chemical nature of the reproductive passages of the females, so that in one strain the Y-bearing sperm were advantaged, in the other the X-bearing.

No progress has been made in respect of the identification of the sex of the unborn child.

PROFESSOR F. A. E. CREW, M.D., D.SC., PH.D.,
F.R.C.P.E.D., F.R.S.

Recurrent Pyrexia of Uncertain Origin

QUERY.—A married female patient, aged twenty-eight, whose childhood was spent in India, suffered some fifteen years ago from malignant malaria. This was "cured" and she had no relapse for over ten years. Twelve months after her return to this country in 1945 she had what to all appearances was an attack of malaria—headache, rigor and malaise, but a temperature that rose to 103° to 104° F. (39.4° to 40° C.) at varying intervals during the succeeding seven days, and finally settled completely. No abnormal physical signs were found and she was put on to a full course of mepacrine. Despite this her attacks continued at intervals of three to four weeks, the severity of the attacks diminishing at each attack and lasting from two to four days. On two occasions during the pyrexial period she was admitted to hospital and repeated blood examinations were carried out. At no time could any organisms be found, and her urine has always been sterile to culture.

After ten to twelve of these attacks she went for a month with no recrudescence and I hoped that the condition was cured. Two further attacks have occurred, however, during the past month and I am at a loss as to the diagnosis or a further line of treatment. Relapsing fever has certainly crossed my mind but the house and the patient are scrupulously clean. Any suggestions as to a possible diagnosis or further course of action would be gratefully received.

REPLY.—Exposure of quite a large section of the population of this country to various tropical diseases in recent years has made the diagnosis of recurrent pyrexia of uncertain origin even more difficult than it sometimes was before the war. Malaria, of course, is by far the most common tropical disease causing recurrent pyrexia. Some patients, even if they had not been taking mepacrine while in an endemic area, appear to develop their first clinical attack when they return to this country, often after a lapse of several months. This applies to benign tertian malaria (*Plasmodium vivax*) but not to malignant or subtertian (*Plasmodium falciparum*). It is thought that the sporozoites of *Plasmodium vivax* first invade fixed-tissue cells in the body and set up a tissue-phase which itself causes no signs of disease. This phase may persist for an unknown period of time, certainly up to three years. From time to time forms of parasites are developed from this tissue-phase which are able to invade the red blood cells. These forms are responsible for clinical attacks of malaria, both the primary attack and the subsequent "relapses". *Plasmodium falciparum* sporozoites also have a tissue-phase, but this seems to terminate with the development of the erythrocytic phase. When untreated, malignant tertian malaria may persist by continuance of the infection in the red blood cells, but once that is eradicated the disease does not relapse like benign tertian malaria. Knowledge of this behaviour of benign tertian malaria has a danger: malaria may be diagnosed when the real cause of the recurrent pyrexia is something quite different. The secret is to find the parasites in the blood. This may not be easy, particularly in relapses. A prolonged search through thin and thick blood films taken every four hours throughout the febrile period is often required.

From the description, the case referred to is probably one of malaria. It is of course assumed, although details are not given, that other "non-tropical" causes of recurrent fever have been carefully excluded, both by clinical and by laboratory investigations. These causes need not be enumerated here, but they can often be remarkably difficult to recognise. Other "tropical" causes are unlikely. The story is not

that of amœbiasis or of kala-azar. Relapsing fever can be dismissed: the disease is virtually unknown in this country and would not appear for the first time so long after the return of the patient to England. If the patient has malaria, for reasons already given the infection would not be related to the attack of malignant tertian malaria she had fifteen years ago. It would be the result of an unrecognized infection with benign tertian parasites at a much more recent date. If the diagnosis can be proved, suitable treatment at the beginning of an attack of fever would be to give a mixture containing 10 grains (0.65 gm.) of quinine sulphate and 10 minims (0.6 c.cm.) of dilute sulphuric acid in one ounce (28.4 c.cm.) of water, three times a day after food for three days. This should be followed by 0.1 gm. of mepacrine, thrice daily for another five days, the first day of mepacrine overlapping with the last day of quinine. After this, 0.1 gm. of paludrine might be given 0.1 gm. a week for at least six months. The paludrine should avert relapses while it is being given and might ultimately eradicate the infection from the body. Even if the diagnosis cannot be proved, it would still be reasonable to try the effects of the treatment suggested, provided that all other causes of recurrent pyrexia have so far as possible been excluded.

EDWARD R. CULLINAN, M.D., F.R.C.P.

Chronic Œdema of the Penis

QUERY.—What are the causes of chronic œdema of the penis, of eight years' duration, in a man of forty years of age who has never been abroad? The following tests have been done and were all negative: Wassermann, Kahn and C.D.T.; Lygranum test for lymphogranuloma inguinale; cystoscopy; catheterization of ureters. The blood count was normal. There was a heavy growth of *B. coli* in the urine on culture. The patient has had attacks of cystitis. There is no history or signs of venereal disease; no evidence of induration of the corpora cavernosa; no inguinal adenitis; no mechanical reason found.

REPLY.—The true diagnosis would seem to lie between: (1) intra-urethral disease; (2) allergy; (3) chronic genital lymphœdema. The possibility of intra-urethral disease as a chronic urethritis should be investigated by means of repeated morning smears, urethroscopy and an examination of the prostatic-vesicular secretion. In view of the several attacks of cystitis due to *B. coli* without any cause for this being found in the bladder or kidneys, the possibility of a chronic focus in the glands of Littre must be considered. Although the negative Lygranum test, and the fact that the patient has never left England, probably exclude lymphogranuloma

inguinale, a complement fixation test might be performed as a check. A Ducrey skin test (Ito Riensterna reaction) would finally eliminate past chancroidal bubo. In spite of the fact that there is no eosinophilia, allergic causes cannot be finally ruled out unless routine skin tests are done. In addition, patch tests, using rubber and material from any quinine or other chemical contraceptives employed by the consort, are worthy of consideration. Indeed the consort herself might with advantage be examined.

Chronic genital lymphœdema is a peculiar affection which is characterized by genital œdema, but the responsible agent is unknown. This is a likely cause in this case. Diagnosis must of necessity be one of exclusion. It is important to know whether the œdema affects the whole penis and scrotum or is confined to the foreskin. Purely local œdema of the prepuce may be due to a fibrotic condition at the frœnum which will be relieved by circumcision. If the œdema affects the whole penis and the scrotum as well, the treatment is still surgical, if the severity warrants this, and excision of the elephantoid tissue may result in a cure.

R. R. WILLCOX, M.B., B.S.

Parpanit and Neurotrasentin in Parkinson's Disease

QUERY.—I would be grateful if you could let me have any information about the following drugs which the "Parkinson Club" seem to have brought to the notice of their members suffering with paralysis agitans:—(1) Parpanit—a Swiss preparation; (2) Neurotrasentin.

REPLY.—Parpanit is the name given by the Swiss firm of J. R. Geigy S.A. of Basle to the chemical compound having the formula Hydrochloride of 1-phenyl-cyclo-pentane-1-carboxylic acid diethylaminoethyl-ester. This preparation has been used in Switzerland in the treatment of various forms of involuntary movements. In Parkinson's disease control or abolition of rigidity is claimed; tremor is less effectively controlled. The recommended dosage lies between 0.025 gm. and 0.075 gm. three to six times daily.

Neurotrasentin is a combination of phenobarbitone with trasentin prepared by Ciba Laboratories Ltd. Trasentin has the composition hexahydrodiphenyl-acetyl-diethyl-amino-ethanol-ester hydrochloride. This drug acts on smooth muscle and inhibits its contraction. It has no noticeable effect on striated muscle, and any effect on the central nervous system is likely to be due to the content of phenobarbitone. Neurotrasentin does not appear to have any effect on the symptoms of Parkinson's disease.

DAVID KENDALL, D.M., M.R.C.P.

PRACTICAL NOTES

Guest Passenger Injuries

THIS is the name given by C. L. Straith (*Journal of the American Medical Association*, May 22, 1948, 137, 348) to the injuries sustained in motor car accidents by passengers sitting in the front seat beside the driver. According to this observer, this is the most dangerous seat in a motor car, and occupants of this "death seat" are said to be injured in the proportion of 3 to 1, compared with drivers. An analysis of 372 persons injured in 289 cars carrying passengers showed that 248 (69 per cent.) of these were riding in the front seat. More than one-half of these suffered head injuries. These head injuries are divided into three main groups:—In the first group are those cases in which the passenger is thrown into the windscreen, resulting in severe injuries from the broken jagged glass. The second group consists of those in which the passenger is thrown into the windscreen and the head is deflected downward on to the dashboard. This results in both cutting and crush injuries, and in children teeth are often dislodged. The third group consists principally of infants and children, and here the head is driven against the dashboard, with resulting crush and tear injuries.



To reduce the incidence of such injuries it is recommended that all knobs, cranks, drop-down ashtrays, sharp ledges, and the like should be removed from the dashboard, and that rubber crash padding should be incorporated in the dashboard in front of the "guest passenger". In addition, it is urged that particular care should be taken with infants and children. They should be held firmly if riding in the front seat and should not be allowed to stand.

The Seasonal Variation in Blood Counts

A STUDY of the blood count in 40 male and 29 female healthy medical students at different seasons of the year is reported by J. Engelbreth-Holm, and Aa. Videbaek of Copenhagen (*Blood*, May 1948, 3, 612). The examinations, which were made four times in one year—in January, March, June and October—consisted of haemoglobin estimations, red cell counts, reticulocyte counts, total and differential white cell counts

and sedimentation rate estimation. It was found that the haemoglobin was lowest in October, the number of reticulocytes highest in June, and the sedimentation rate lowest in June. No statistically significant difference was found in the red cell count or in the total or differential white cell count. The following are the significant findings as averages:—

MALES

	January	March	June	October
Red cells (millions)	5.06	4.94	5.00	4.96
Haemoglobin (per cent.)	100	97	99	89
Colour index	0.99	0.98	0.99	0.90
Reticulocytes (per 1000 erythrocytes)	4.2	4.2	5.8	4.6
Sedimentation rate	2.6	2.5	2.2	3.0

FEMALES

	January	March	June	October
Red cells (millions)	4.41	4.40	4.32	4.24
Haemoglobin (per cent.)	86	84	84	77
Colour index	0.97	0.95	0.97	0.91
Reticulocytes (per 1000 erythrocytes)	4.5	3.4	5.0	4.7
Sedimentation rate	5.2	4.5	3.6	5.4

The Nitrogen Mustards in Clinical Use

A RECORD of the results obtained by the administration of nitrogen mustards to over 300 patients at the Memorial Hospital, New York, between October 1944 and December 1947, is made by L. Craver (*Radiology*, April 1948, 50, 486). The cases treated included Hodgkin's disease (102), lymphosarcoma (66), leukaemia (65), carcinoma (48), including 33 of the lung, and sarcoma (16). The substance most generally used was methyl-bis(beta-chlorethyl)amine hydrochloride, the customary dosage being 0.1 mgm. per kgm. body weight, once daily for four days, but in some cases going on to six, seven or even more single doses. In some instances an initial dose of 0.05 mgm. per kgm. body weight was used. The dosage is guided largely by the total white cell count. Latterly, the double-dose system was employed, i.e. 0.2 mgm. per kgm. body weight on two successive days, followed in some cases by a similar dose on the third, fourth and fifth days. Great care is needed when giving the injections to avoid introduction of the slightest amount of nitrogen mustard into the tissue outside the veins; thus it is advisable to perform the venepuncture with the needle attached to a

that of amœbiasis or of kala-azar. Relapsing fever can be dismissed: the disease is virtually unknown in this country and would not appear for the first time so long after the return of the patient to England. If the patient has malaria, for reasons already given the infection would not be related to the attack of malignant tertian malaria she had fifteen years ago. It would be the result of an unrecognized infection with benign tertian parasites at a much more recent date. If the diagnosis can be proved, suitable treatment at the beginning of an attack of fever would be to give a mixture containing 10 grains (0.65 gm.) of quinine sulphate and 10 minims (0.6 c.cm.) of dilute sulphuric acid in one ounce (28.4 c.cm.) of water, three times a day after food for three days. This should be followed by 0.1 gm. of mepacrine, thrice daily for another five days, the first day of mepacrine overlapping with the last day of quinine. After this, 0.1 gm. of paludrine might be given once a week for at least six months. The paludrine should avert relapses while it is being given and might ultimately eradicate the infection from the body. Even if the diagnosis cannot be proved, it would still be reasonable to try the effects of the treatment suggested, provided that all other causes of recurrent pyrexia have so far as possible been excluded.

EDWARD R. CULLINAN, M.D., F.R.C.P.

Chronic Œdema of the Penis

QUERY.—What are the causes of chronic œdema of the penis, of eight years' duration, in a man of forty years of age who has never been abroad? The following tests have been done and were all negative: Wassermann, Kahn and C.D.T.; Lygranum test for lymphogranuloma inguinale; cystoscopy; catheterization of ureters. The blood count was normal. There was a heavy growth of *B. coli* in the urine on culture. The patient has had attacks of cystitis. There is no history or signs of venereal disease; no evidence of induration of the corpora cavernosa; no inguinal adenitis; no mechanical reason found.

REPLY.—The true diagnosis would seem to lie between: (1) intra-urethral disease; (2) allergy; (3) chronic genital lymphœdema. The possibility of intra-urethral disease as a chronic urethritis should be investigated by means of repeated morning smears, urethroscopy and an examination of the prostatic-vesicular secretion. In view of the several attacks of cystitis due to *B. coli* without any cause for this being found in the bladder or kidneys, the possibility of a chronic focus in the glands of Littre must be considered. Although the negative Lygranum test, and the fact that the patient has never left England, probably exclude lymphogranuloma

inguinale, a complement fixation test might be performed as a check. A Ducrey skin test (Itti-Rienstierna reaction) would finally eliminate past chancroidal bubo. In spite of the fact that there is no eosinophilia, allergic causes cannot be finally ruled out unless routine skin tests are done. In addition, patch tests, using rubber and material from any quinine or other chemical contraceptives employed by the consort, are worthy of consideration. Indeed the consort herself might with advantage be examined.

Chronic genital lymphœdema is a peculiar affection which is characterized by genital œdema, but the responsible agent is unknown. This is a likely cause in this case. Diagnosis must of necessity be one of exclusion. It is important to know whether the œdema affects the whole penis and scrotum or is confined to the foreskin. Purely local œdema of the prepuce may be due to a fibrotic condition at the frenum which will be relieved by circumcision. If the œdema affects the whole penis, and the scrotum as well, the treatment is still surgical, if the severity warrants this, and excision of the elephantoid tissue may result in a cure.

R. R. WILLCOX, M.B., B.S.

Parpanit and Neurotrasentin in Parkinson's Disease

QUERY.—I would be grateful if you could let me have any information about the following drugs which the "Parkinson Club" seem to have brought to the notice of their members suffering with paralysis agitans:—(1) Parpanit—a Swiss preparation; (2) Neurotrasentin.

REPLY.—Parpanit is the name given by the Swiss firm of J. R. Geigy S.A. of Basle to the chemical compound having the formula: Hydrochloride of 1-phenyl-cyclo-pentane-1-carboxylic acid diethylaminoethylester. This preparation has been used in Switzerland in the treatment of various forms of involuntary movements. In Parkinson's disease control or abolition of rigidity is claimed; tremor is less effectively controlled. The recommended dosage lies between 0.025 gm. and 0.075 gm. three to six times daily.

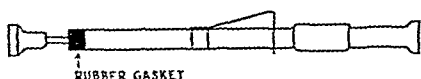
Neurotrasentin is a combination of phenobarbitone with trasentin prepared by Ciba Laboratories Ltd. Trasentin has the composition hexahydrodiphenyl-acetyl-diethyl-aminoethanolester hydrochloride. This drug acts on smooth muscle and inhibits its contraction. It has no noticeable effect on striated muscle, and any effect on the central nervous system is likely to be due to the content of phenobarbitone. Neurotrasentin does not appear to have any effect on the symptoms of Parkinson's disease.

DAVID KENDALL, D.M., M.R.C.P.

that it may be rash to ascribe improvement to the treatment alone. No theories are advanced as to the mechanism of action of folic acid, but its use is advocated in this disease for which no effective treatment has yet been found.

1 Modified Automatic Blood Lancet

MODIFICATION of the ordinary automatic blood lancet is described by L. C. Clark, Jun. (*American Journal of Clinical Pathology*, May 1948, 18, 442). The disadvantage of the spring lancet for finger puncture in general use is that the blade remains extended after the puncture has been made, thus increasing the pain and adding to the difficulty of obtaining blood samples, particularly in children. In the modified instrument described the blade springs back flush with the surface of the skin "fraction of a second after penetration".



Conversion of an ordinary spring lancet can easily be done by placing a rubber gasket between the stopping knob and the end of the lancet body, the gasket being made by cutting a piece of rubber tubing of the correct size and elasticity; or the end of a size 1A-66F vaccine bottle stopper can be cut for the purpose. The gasket is fixed by unscrewing the knob at the end of the lancet shaft, slipping the gasket (which should be 4 to 5 mm. thick) on, and tightening the knob. The actual thickness of the gasket used should depend upon the tension of the driving spring of the lancet used and upon the depth of the cut required. Another advantage claimed is that the gasket muffles the click of the lancet, which may frighten infants and young children. It is stated that the new modification "was reported to be nearly painless by those subjects who were tested".

Liver Biopsy in Hepatic Bilharziasis

LIVER biopsy has been used for the diagnosis of hepatic bilharziasis in a series of forty-one cases by M. Erfan and S. Talaat (*Journal of the Royal Egyptian Medical Association*, December 1947, 30, 663). The method employed was as follows:—

With the patient lying supine in bed with the right side as near the edge as possible and the right arm behind the head, a site is chosen in the ninth intercostal space in the middle or anterior axillary line. After sterilization the skin is anesthetized with 2 per cent. novocain solution, a total of 10 c.cm. being used. Using a long fine-bore needle the pleura and peritoneal covering of the liver are infiltrated, and then a small-calibre lumbar puncture needle, with bevelled tip to act as trocar and cannula, is pushed 2-3 cm. deep into the liver, with the patient in full expiration. The trocar is withdrawn and a 10 c.cm. record syringe is fitted tightly to the end of the cannula. Suction is applied and the cannula pushed in a further 2-4 cm., and then withdrawn while suction is maintained.

The skin puncture is sealed with collodion. The liver substance obtained is washed in saline and transferred to a centrifuge tube; five drops of 4 per cent. sodium hydroxide are added, the tube is warmed over a burner until the material is totally digested, and then centrifuged. The deposit is examined microscopically for schistosoma ova.

Of the forty-one cases examined schistosoma ova were obtained from the liver substance in twenty-one. In three cases *S. haematobium* only were present in the liver and faeces, showing that *S. haematobium* alone may cause hepatic bilharziasis. In seven of the twenty-one cases in which schistosoma ova were present in the liver none was found in the faeces, thus indicating the value of liver biopsy in those cases in which the faeces are negative for schistosoma. In thirty-nine of the forty-one cases bilharzia ova were present in liver, faeces or urine; and in nineteen of the twenty-one cases with bilharzia ova in the stools there was enlargement of the liver and spleen, showing that hepatic bilharziasis is almost invariably present with intestinal bilharziasis. In one case with no enlargement of the liver or spleen, bilharzia ova were present in the liver.

Calcium Gluconate for the Relief of Pleural Pain

As a result of their experiences in thirty patients I. L. Bennett, Jun. and W. Lathem (*American Journal of the Medical Sciences*, April 1948, 215, 431) recommend the intravenous administration of calcium gluconate for the relief of pleural pain. All thirty patients had "acute pleuritic pain due to either pneumonia or pulmonary infarction". The calcium gluconate was given intravenously in the form of 10 to 20 c.cm. of a 10 per cent. solution. Two to four minutes were taken for each injection. Only two side-effects were noted: a sense of warmth and flushing, and occasional mild nausea. The drug was not given to patients receiving digitalis. Relief of pain was obtained in twenty-seven of the patients, although in only four of these was the relief permanent. Relief was evident within 60 seconds of the beginning of the injection, and this was accompanied by easing of the tenderness and hyperalgesia of the chest wall and upper abdominal muscles. When the pain recurred, it usually did so in 30 to 60 minutes. In ten patients a second injection of the drug gave further relief. "The practical value of the use of calcium gluconate [it is claimed] lies in its simplicity". Most of the patients in this series subsequently obtained more lasting relief from procaine block of the intercostal nerves or by ethyl chloride spray. Incidentally, it is suggested that these results with calcium gluconate support the theory that the pain associated with pleurisy is due to painful spasm of the intercostal muscles.

syringe containing saline solution, then change to that containing the nitrogen mustard, and then back to the syringe containing saline. Or, as preferred by some, the nitrogen mustard may be injected into the tube of an infusion set through which a small infusion of glucose or saline solution is running rather rapidly. The author's conclusions, based on the results obtained in the series, are: (1) None of the nitrogen mustards so far used has given any indication of being curative in any type of cancer. (2) In certain types of cancer, however, the palliative effects of nitrogen mustard have been marked, i.e., in cases of Hodgkin's disease with marked constitutional symptoms, which often respond rapidly to nitrogen mustard therapy. (3) It seems doubtful if, in general, nitrogen mustard therapy offers any advantage over other types of treatment, and particularly X-ray therapy, in Hodgkin's disease in the early and intermediate stages, in lymphosarcoma, and in chronic leukaemia. Nevertheless, in two cases of carcinoma of the lung there was a dramatic response: in one patient, rapidly going downhill and expected to die within two to three weeks, relief of symptoms occurred within a few days. A second case responded similarly. The remissions were only partial, however, but could be extended by million-volt X-ray therapy to the intrathoracic part of the tumour. In the author's words: "As a means of palliation of anaplastic cancer of the lung, this combination of HN₂ followed by X-ray therapy has seemed worth while".

Platelet Counts to Control Radiotherapy

THE use of platelet counts in controlling wide-field X-ray therapy is recommended by W. M. Court Brown (*British Journal of Radiology*, May 1948, **21**, 221) on the grounds that "the blood platelet level is a more reliable indication of the effect of radiation on the bone marrow than the total white cell count". This recommendation is based upon observations made in over a hundred cases, as a result of which it is claimed that "it can be definitely stated that by using the platelet count in this manner it is possible to avoid altogether the production of undesired constitutional effects from excessive irradiation of the hæmopoietic system, and yet at the same time administer adequate dosage". The standards that have been adopted are that a level of 200,000 platelets per c.mm. has been taken as the lower limit of normal, and that a level of 100,000 per c.mm. has been adopted as the lower limit of safety. A platelet count was done before the institution of treatment and then on every third day during treatment.

Attention is drawn to the fact that accurate and constant results can be obtained only after considerable practice, and even then are dependent upon the use of a good microscope.

Amidone (Methadon) in Occlusive Arterial Disease

THE results of the use of methadon as an analgesic in 28 patients with occlusive arterial disease associated with marked ischaemic pain are reported by R. J. Popkin (*American Heart Journal*, May 1948, **35**, 793). The usual dose was 5 to 15 mgm. in tablet or capsule form, but occasionally it was given intramuscularly, 5 mgm. being dissolved in each cubic centimetre of distilled water. In only two patients was no relief from pain obtained. In the majority the relief of pain was prompt and satisfactory, and persisted for up to sixteen hours. There was no effect upon intermittent claudication or the pain brought on by dependency or weight bearing. Although it is now recognized that this drug has definite habit-forming propensities, and should therefore be used with corresponding caution, there was no evidence of addiction or of increase in tolerance in this small series. Constipation was a rare complaint. Unpleasant side-effects were frequent in ambulant cases but few in recumbent cases. Light-headedness, nausea or vomiting occurred in "a large percentage of cases" when sitting, standing or walking. In some patients these symptoms were severe enough to prevent further administration of the drug. Occasionally patients could not tolerate the drug, even in the recumbent position. In one patient, with a previous history of allergic reactions, a hæmorrhagic urticaria developed after the administration of 925 mgm. of methadon over a period of seventeen days.

Porphyria and Folic Acid

IN two cases of porphyria treated with folic acid, 20 mgm. daily by mouth, by M. R. Castex, A. L. García, and J. F. Zelasco (*Prensa Médica Argentina*, May 14, 1948, **35**, 907) marked improvement resulted. The first patient, a woman aged twenty-five, had had obstinate cutaneous porphyria for three years. This was considerably improved within one month. Treatment was continued with 10 mgm. folic acid daily for ten days, followed by injections of vitamin B complex for ten days, and hepatic extract by mouth for ten days. The skin condition cleared completely. The second patient, a woman of thirty, was diagnosed as cholelithiasis. Porphyria was found, and marked improvement followed folic acid therapy. The authors point out that porphyria is a condition characterized by spontaneous remissions,

into one place the known facts concerning the human infection, giving a detailed account of the morphology and cultural requirements of the vaginal parasite, summarizing the experimental work of clinicians and laboratory workers, and reviewing the many methods of treatment which have been tried. Dr. Trussell and his colleagues have themselves contributed greatly to this investigation by a series of important studies with pure subcultures of the organism, with which they seem to have been first in the field. All aspects of this subject come under discussion, including the important question of the relationship of the vaginal parasite to the similar organisms which are found in the human mouth and the human intestinal tract. The book is full of information and well written, but is marred here and there by errors in spelling due to faulty proof-reading. The list of references is practically complete and must prove most valuable. All who treat this common and troublesome condition, whether consultants or practitioners, will find this volume of absorbing interest and a source of valuable ideas for the treatment of resistant and relapsing cases.

NEW EDITIONS

THE eighth edition of *Handbook of Practical Bacteriology*, by T. J. Mackie, C.B.E., M.D., D.P.H., and J. E. McCartney, M.D., D.Sc. (E. & S. Livingstone Ltd., 25s.) has been completely revised. New features include a section on the antibiotics; the agglutination tests are described in detail, and a section is devoted to the B.C.G. strain of tubercle bacillus and its use for the production of immunity.

THE many advances in cardiology that have taken place since the appearance of the previous edition of *Recent Advances in Cardiology*, by Terence East, D.M., F.R.C.P., and Curtis Bain, M.C., D.M., F.R.C.P., have necessitated complete rewriting in the preparation of the fourth edition (J. & A. Churchill Ltd., 24s.). Among new additions are the use of the sulphonamides in rheumatic heart disease; penicillin in the treatment of bacterial endocarditis; the surgical treatment of congenital pulmonary stenosis, and thiouracil in the treatment of angina pectoris and the cardiac symptoms of hyperthyroidism. An entire chapter is devoted to cardiography.

Cardiovascular Diseases: Their Diagnosis and Treatment, by David Scherf, M.D., F.A.C.P., and Linn J. Boyd, M.D., F.A.C.P., in its second edition (Wm. Heinemann [Medical Books] Ltd., 63s.) has been completely rewritten. A chapter is devoted to rheumatic fever, and in the chapter on non-rheumatic endocarditis treatment with the sulphonamides and penicillin in conjunction

with heparin and hyperthermia is discussed. Each chapter in the new edition concludes with an excellent bibliography.

Principles of Medical Statistics, by A. BRADFORD Hill, D.Sc., Ph.D., in its fourth edition (Lancet Ltd., 10s. 6d.) contains a new chapter on the calculation of averages, and other sections have been revised and extended. As a guide to the efficiency of different forms of treatment, the incidence of diseases, mortality rates, and other subjects connected with public health this work will be found of considerable value.

The Anatomy of the Eye and Orbit, by Eugene Wolff, M.B., B.S., F.R.C.S., in its third edition (H. K. Lewis & Co. Ltd., 45s.) has been enriched by the inclusion of eighty new illustrations, bringing the total up to 323; they are beautifully produced. The work is too well known to call for detailed description.

A SECTION on erythroblastosis foetalis is among the new additions to *A Manual of Practical Obstetrics*, by O'Donel Browne, M.B., M.A.O., F.R.C.P.I., F.R.C.O.G., in its second edition (John Wright & Sons Ltd., 35s.), and there is a useful chapter on antenatal care in which a suggested diet is included. The new edition is well illustrated with 218 figures and 8 plates.

IN the preparation of the second edition of *An Introduction to Physical Methods of Treatment in Psychiatry*, by William Sargent, M.B., M.R.C.P., D.P.M., and Eliot Slater, M.D., F.R.C.P., D.P.M. (E. & S. Livingstone Ltd., 10s. 6d.) considerable new material has been added, particularly in the sections devoted to insulin therapy, convulsive therapy, prefrontal leucotomy, and the use of drugs in psychotherapy; and there is a chapter on the treatment of epilepsy by Denis Hill. The new edition of this work, which so admirably combines the physical and psychotherapeutic treatment of mental disorders, will be warmly welcomed.

THOROUGH revision has been undertaken in the preparation of *A Text-Book of Midwifery*, by R. W. Johnstone, C.B.E., M.D., F.R.C.S.E., M.R.C.P.E., F.R.C.O.G., F.R.S.E., in its thirteenth edition (A. & C. Black, 30s.), and a new section on the Rhesus factor has been added. A separate section has been devoted to vomiting in pregnancy, and much new information on antenatal care is included.

Dietetics in General Practice, by Leslie Cole, M.D., F.R.C.P., in its second edition (Staples Press Ltd., 8s. 6d.) contains some useful diets. There are also chapters dealing with the subjects of under- and over-nutrition, infant feeding, and food allergy.

REVIEWS OF BOOKS

The Practice of Industrial Medicine. By T. A. LLOYD DAVIES, M.D., M.R.C.P. London: J. & A. Churchill Ltd., 1948. Pp. vii and 244. Figures 8 and tables 20. Price 15s.

A CHAPTER on industrial disease and toxicology forms half the contents of this book. The more important industrial diseases are dealt with clearly and briefly. There is a short chapter of eleven pages on the hazards of coal mining, by a mines medical officer. The remainder of the book includes chapters on the medical examination, the social functions of industry, accidents, fatigue and environment, workmen's compensation, and rehabilitation. The objectives of industrial medicine, an historical survey and the future are dealt with too briefly in seven pages. The title is misleading, as this book is an entertaining and readable account of the author's reaction to human problems in industry, rather than an outline of modern methods of industrial medical practice. Nevertheless, it will be of interest to industrial medical officers and nurses.

American Medical Research Past and Present. By RICHARD H. SHYROCK, Ph.D. London: Oxford University Press, 1947. Pp. xiv and 350. Price 14s.

THIS is the latest of the series of monographs issued under the auspices of the Committee on Medicine and the Changing Order of the New York Academy of Medicine. As an account of the development of medical research in America during the last two hundred years it makes stimulating and interesting reading. The history of the development of medical research in America is a very different one from that in Great Britain. Names such as Rockefeller, Carnegie and Harkness are such household ones in the sphere of medical research that it is sometimes forgotten how comparatively recently these magnates of the business world came to the rescue of research. As an historical record this monograph makes fascinating reading, but it must be confessed that when it embarks upon the perilous sea of the philosophical basis of research it makes heavy going. Research, whether medical or otherwise, has a three-fold justification: as an intellectual exercise, as a search after truth, and as a means of improving the physical and material well-being of humanity. To attempt to suggest that these three viewpoints are incompatible is entirely unjustified. But it is equally unjustified to suggest, as is done in this work, that the third viewpoint is either the only, or even the principal, justifica-

tion for its existence. We in Great Britain may tend to err in the opposite direction, but it will be a bleak day for humanity when research is judged merely on the materialistic basis of the practical results it produces. Fortunately this monograph is not written as a piece of special pleading, and all who are interested in medical research will benefit from a careful study of its pages.

Modern Trends in Ophthalmology. Volume 2. EDITED BY ARNOLD SORSBY, M.D., F.R.C.S. London: Butterworth & Co. (Publishers) Ltd., 1938. Pp. xix and 600. Figures 169 and 3 colour plates. Price 63s.

IN the preface to this volume Professor Sorsby states that he has attempted to fill the gap in the preceding one and to indicate the developments that have occurred since the publication of the first volume seven years ago. The subject matter is divided into five sections—Physiology, Diagnostic Procedures, Pathology, Treatment, and Social Aspects. The editor contributes chapters on X-ray measurement of the diameters of the living eye, virus infections, sulphonamides, penicillin and amniotic membrane grafts. The subjects dealt with and their manner of treatment comprise a mixture of the practical, the academic and the learned, and the editor has cast far afield in his choice of authors. It is impossible to treat fairly a book such as this in a short review: important articles are recognized at once in Granit's chapter on the electrophysiology of the retina; Stenström's on the optical components of the eye; Björk's on hypertensive retinopathy; and Dorothy Campbell's on industrial ophthalmology. An important and valuable volume, and a worthy successor, which every progressive ophthalmologist must possess.

Trichomonas Vaginitis and Trichomoniasis. By RAY E. TRUSSELL, M.D. Oxford: Blackwell Scientific Publications Ltd., 1948. Pp. xii and 277. Figures 25. Price 30s.

TRICHOMONAS vaginitis has been recognized for more than 100 years as a troublesome infection which is often resistant to treatment. The causative organism was discovered by Donné as long ago as 1836, but much remains to be learnt about the fundamental pathology of the disease. The author of this book has done a notable service to those who study and treat the conditions which are caused by this protozoon and its near neighbours. He has gathered

into one place the known facts concerning the human infection, giving a detailed account of the morphology and cultural requirements of the vaginal parasite, summarizing the experimental work of clinicians and laboratory workers, and reviewing the many methods of treatment which have been tried. Dr. Trussell and his colleagues have themselves contributed greatly to this investigation by a series of important studies with pure subcultures of the organism, with which they seem to have been first in the field. All aspects of this subject come under discussion, including the important question of the relationship of the vaginal parasite to the similar organisms which are found in the human mouth and the human intestinal tract. The book is full of information and well written, but is marred here and there by errors in spelling due to faulty proof-reading. The list of references is practically complete and must prove most valuable. All who treat this common and troublesome condition, whether consultants or practitioners, will find this volume of absorbing interest and a source of valuable ideas for the treatment of resistant and relapsing cases.

NEW EDITIONS

THE eighth edition of *Handbook of Practical Bacteriology*, by T. J. Mackie, C.B.E., M.D., D.P.H., and J. E. McCartney, M.D., D.Sc. (E. & S. Livingstone Ltd., 25s.) has been completely revised. New features include a section on the antibiotics; the agglutination tests are described in detail, and a section is devoted to the B.C.G. strain of tubercle bacillus and its use for the production of immunity.

THE many advances in cardiology that have taken place since the appearance of the previous edition of *Recent Advances in Cardiology*, by Terence East, D.M., F.R.C.P., and Curtis Bain, M.C., D.M., F.R.C.P., have necessitated complete rewriting in the preparation of the fourth edition (J. & A. Churchill Ltd., 24s.). Among new additions are the use of the sulphonamides in rheumatic heart disease; penicillin in the treatment of bacterial endocarditis; the surgical treatment of congenital pulmonary stenosis, and thiouracil in the treatment of angina pectoris and the cardiac symptoms of hyperthyroidism. An entire chapter is devoted to cardiography.

Cardiovascular Diseases: Their Diagnosis and Treatment, by David Scherf, M.D., F.A.C.P., and Linn J. Boyd, M.D., F.A.C.P., in its second edition (Wm. Heinemann [Medical Books] Ltd., 63s.) has been completely rewritten. A chapter is devoted to rheumatic fever, and in the chapter on non-rheumatic endocarditis treatment with the sulphonamides and penicillin in conjunction

with heparin and hyperthermia is discussed. Each chapter in the new edition concludes with an excellent bibliography.

Principles of Medical Statistics, by A. BRADFORD Hill, D.Sc., Ph.D., in its fourth edition (Lancet Ltd., 10s. 6d.) contains a new chapter on the calculation of averages, and other sections have been revised and extended. As a guide to the efficiency of different forms of treatment, the incidence of diseases, mortality rates, and other subjects connected with public health this work will be found of considerable value.

The Anatomy of the Eye and Orbit, by Eugene Wolff, M.B., B.S., F.R.C.S., in its third edition (H. K. Lewis & Co. Ltd., 45s.) has been enriched by the inclusion of eighty new illustrations, bringing the total up to 323; they are beautifully produced. The work is too well known to call for detailed description.

A SECTION on erythroblastosis foetalis is among the new additions to *A Manual of Practical Obstetrics*, by O'Donel Browne, M.B., M.A.O., F.R.C.P.I., F.R.C.O.G., in its second edition (John Wright & Sons Ltd., 35s.), and there is a useful chapter on antenatal care in which a suggested diet is included. The new edition is well illustrated with 218 figures and 8 plates.

IN the preparation of the second edition of *An Introduction to Physical Methods of Treatment in Psychiatry*, by William Sargant, M.B., M.R.C.P., D.P.M., and Eliot Slater, M.D., F.R.C.P., D.P.M. (E. & S. Livingstone Ltd., 10s. 6d.) considerable new material has been added, particularly in the sections devoted to insulin therapy, convulsive therapy, prefrontal leucotomy, and the use of drugs in psychotherapy; and there is a chapter on the treatment of epilepsy by Denis Hill. The new edition of this work, which so admirably combines the physical and psychotherapeutic treatment of mental disorders, will be warmly welcomed.

THOROUGH revision has been undertaken in the preparation of *A Text-Book of Midwifery*, by R. W. Johnstone, C.B.E., M.D., F.R.C.S.E., M.R.C.P.E., F.R.C.O.G., F.R.S.E., in its thirteenth edition (A. & C. Black, 30s.), and a new section on the Rhesus factor has been added. A separate section has been devoted to vomiting in pregnancy, and much new information on antenatal care is included.

Dietetics in General Practice, by Leslie Cole, M.D., F.R.C.P., in its second edition (Staples Press Ltd., 8s. 6d.) contains some useful diets. There are also chapters dealing with the subjects of under- and over-nutrition, infant feeding, and food allergy.

NOTES AND PREPARATIONS

NEW PREPARATIONS

CHRONALGIN (urea 20 per cent., ephedrine sulphate 1 per cent., silver proteinate 10 per cent., phenyl mercuric nitrate 0.1 per cent., mono phenyl ether of ethylene glycol 2 per cent., industrial methylated spirit, 10 per cent.) has been prepared for the treatment of chronic suppurative otitis media. It is issued in bottles of 25 and 100 c.cm., price 5s. and 16s. 10d., less professional discount, by Benger's Limited, Holmes Chapel, Cheshire.

HEPARIN (EVANS), stated to be a pure, pyrogen-free heparin product, is available in the form of solutions of 5000 I.U. and 1000 I.U. per c.cm., in ampoules of 5 c.cm., in powder in glass containers of 100,000 I.U., and also in heparinized tubes of 10 c.cm. containing 100 I.U. in the form of a dried film. A descriptive booklet can be obtained from the manufacturers, Evans Medical Supplies Ltd., Speke, Liverpool 19.

THE ROYAL SOCIETY OF MEDICINE

THE Annual Meeting of the Society was held on July 6, with Sir Maurice Cassidy, President of the Society, in the Chair. The number of Fellows now exceeds 9000, the highest on record. Library statistics show that readers in the library during the past year totalled nearly 47,000, and that over 53,000 books were borrowed for home use. Sir Henry Dale, O.M., F.R.S., was elected President for the ensuing year.

THE BRITISH RHEUMATIC ASSOCIATION

THE Inaugural and First Annual General Meeting of the British Rheumatic Association was held at the Mansion House on June 17, the Lord Mayor presiding. The aims of the Association, which is an organization for patients and their friends for the furtherance of improvements in diagnostic and therapeutic measures and the assistance of individual sufferers, were explained by Col. M. Stoddart-Scott, M.D., M.P., vice-chairman of the council. The address of the British Rheumatic Association, of which Lord Horder is Hon. Vice-President, is 5 Tite Street, Chelsea, London, S.W.3.

A NEW FILM ON POLIOMYELITIS

A NEW film, entitled "Polio: Diagnosis and Management", has been produced for the Ministry by the Crown Film Unit, directed by Geoffrey Innes. The film opens with a diagrammatic presentation of the spread of the virus in one family, and then proceeds to tell the story of one case, from the earliest symptoms to the

late stages of rehabilitation. The film is available in 35 mm. and 16 mm. from the Central Film Library, and on the Mobile Film Units of the Central Office of Information. The address of the Central Film Library is Imperial Institute, London, S.W.7, and in Scotland, 2 Newton Place, Glasgow, C.3.

THE DANISH ASSOCIATION AGAINST TUBERCULOSIS

EARLY in the nineties a comprehensive campaign against tuberculosis was started in Denmark, which covered propaganda and educational work, the building of sanatoria and the State Serum Institute in Copenhagen, where work on the preparation of prophylactic sera is carried out under the leadership of Professor K. A. Jensen. The Danish Red Cross has established a college or hostel in Copenhagen where doctors are given a free three months' course in the elements of combating tuberculosis. The Association extends an invitation to any British doctor interested in the problems of tuberculosis, to see the work being carried on. Application should be made to the National Association against Tuberculosis, 21 Store Strandstraede, Copenhagen. A limited number of scholarships is available to British doctors.

PUBLICATIONS

Immunization against Diphtheria, issued by the Ministry of Health, shows that deaths from diphtheria in 1947 were 245—for the sixth successive year the lowest yet recorded—compared with an average mortality total of about 2,800 annually for the ten-year period 1931-40.

Eat and be Healthy, by Lucius Nicholls, C.M.G., M.D., deals with the subjects of diet and nutrition in Ceylon, and contains some useful charts in colour giving the calories and vitamin contents of foodstuffs. It is obtainable from the Associated Newspapers of Ceylon, Langham House, 302 Regent Street, London, W.1, price 4s. 6d. or 5s. 8d. cloth covered.

Enuresis, a memorandum prepared by the Joint Committee of the British Medical Association and the Magistrates' Association on Psychiatry and the Law, deals with the causes and treatment of enuresis in the child and adult. It is published by the British Medical Association, B.M.A. House, Tavistock Square, London, W.C.1.

The contents of the September issue, which will include a symposium on "The Problem of Rheumatism", will be found on page 151 at the end of the advertisement section.

THE PRACTITIONER

No. 963

SEPTEMBER 1948

Volume 161

THE PROBLEM OF RHEUMATISM

By A. H. DOUTHWAITE, M.D., F.R.C.P.

Physician, Guy's Hospital.

THIS symposium deals with chronic rheumatism. The first problem is to define, or rather to delimit, the term. To some it connotes a much wider field of disease than it does to others. However, the last decade has done much to reduce the number of maladies crowding under its shelter. Thus it is now known that sciatica, associated with the physical signs formerly attributed to sciatic neuritis, is not rheumatic, but the result of a mechanical disturbance in the spine. The same applies to most of the acute agonizing forms of lumbago. Lesions of the intervertebral discs, or strains of the spinal joints account for almost all of these. "*Brachial neuritis*" has also joined the group of mechanically produced diseases, and we are happily no longer obliged to explain the inexplicable, i.e. "neuritis" unassociated with sensory change. Gout is clearly not rheumatism. Is the term gouty rheumatism justifiable? I believe not. It is a slipshod, safety-first term for the use of a hivering diagnostician. Rheumatic purpura and erythema nodosum have long been cast from the fold. We are left with osteoarthritis, rheumatoid arthritis, Still's disease, infective (focal) arthritis, certain forms of spondylitis, palindromic rheumatism, and that dangerously embracing term "fibrositis". The feature common to all except the last is that the lesions are concentrated in or about the joints. Their pathology is, however, diverse, and it is obvious that their causes differ equally. It is safe to forecast that the term "chronic rheumatism" will disappear as knowledge of its component parts increases.

CAUSATION

The next problem, which is also largely unsolved, is to explain the origin of those diseases which for convenience we call *rheumatic*. *Osteoarthritis* is less troublesome than the rest. It can be produced in any joint by repeated trauma. Experimentally this can be done by the introduction of a hard foreign body into the cavity. It arises time and again in joints exposed to abnormal stresses. Thus the knees, ankles, and feet of the obese are commonly attacked. The first metatarso-phalangeal joint was seldom spared in those of the Edwardian and Victorian generations because their feet were forced to fit the shoes; and these were pointed. In parenthesis, this widespread unsightliness of the big toe explains why it is the joint of election

NOTES AND PREPARATIONS

NEW PREPARATIONS

CHRONALGICIN (urea 20 per cent., ephedrine sulphate 1 per cent., silver proteinate 10 per cent., phenyl mercuric nitrate 0.1 per cent., mono phenyl ether of ethylene glycol 2 per cent., industrial methylated spirit, 10 per cent.) has been prepared for the treatment of chronic suppurative otitis media. It is issued in bottles of 25 and 100 c.cm., price 5s. and 16s. 10d., less professional discount, by Benger's Limited, Holmes Chapel, Cheshire.

HEPARIN (EVANS), stated to be a pure, pyrogen-free heparin product, is available in the form of solutions of 5000 I.U. and 1000 I.U. per c.cm., in ampoules of 5 c.cm., in powder in glass containers of 100,000 I.U., and also in heparinized tubes of 10 c.cm. containing 100 I.U. in the form of a dried film. A descriptive booklet can be obtained from the manufacturers, Evans Medical Supplies Ltd., Speke, Liverpool 19.

THE ROYAL SOCIETY OF MEDICINE

THE Annual Meeting of the Society was held on July 6, with Sir Maurice Cassidy, President of the Society, in the Chair. The number of Fellows now exceeds 9000, the highest on record. Library statistics show that readers in the library during the past year totalled nearly 47,000, and that over 53,000 books were borrowed for home use. Sir Henry Dale, O.M., F.R.S., was elected President for the ensuing year.

THE BRITISH RHEUMATIC ASSOCIATION

THE Inaugural and First Annual General Meeting of the British Rheumatic Association was held at the Mansion House on June 17, the Lord Mayor presiding. The aims of the Association, which is an organization for patients and their friends for the furtherance of improvements in diagnostic and therapeutic measures and the assistance of individual sufferers, were explained by Col. M. Stoddart-Scott, M.D., M.P., vice-chairman of the council. The address of the British Rheumatic Association, of which Lord Horder is Hon. Vice-President, is 5 Tite Street, Chelsea, London, S.W.3.

A NEW FILM ON POLIOMYELITIS

A NEW film, entitled "Polio: Diagnosis and Management", has been produced for the Ministry by the Crown Film Unit, directed by Geoffrey Innes. The film opens with a diagrammatic presentation of the spread of the virus in one family, and then proceeds to tell the story of one case, from the earliest symptoms to the

late stages of rehabilitation. The film is available in 35 mm. and 16 mm. from the Central Film Library, and on the Mobile Film Units of the Central Office of Information. The address of the Central Film Library is Imperial Institute London, S.W.7, and in Scotland, 2 Newton Place, Glasgow, C.3.

THE DANISH ASSOCIATION AGAINST TUBERCULOSIS

EARLY in the nineties a comprehensive campaign against tuberculosis was started in Denmark which covered propaganda and educational work, the building of sanatoria and the State Serum Institute in Copenhagen, where work on the preparation of prophylactic sera is carried out under the leadership of Professor K. A. Jensen. The Danish Red Cross has established a college or hostel in Copenhagen where doctors are given a free three months' course in the elements of combating tuberculosis. The Association extends an invitation to any British doctor interested in the problems of tuberculosis, to see the work being carried on. Application should be made to the National Association against Tuberculosis, 21 Store Strandstraede, Copenhagen. A limited number of scholarships is available to British doctors.

PUBLICATIONS

Immunization against Diphtheria, issued by the Ministry of Health, shows that deaths from diphtheria in 1947 were 245—for the sixth successive year the lowest yet recorded—compared with an average mortality total of about 2,800 annually for the ten-year period 1931-40.

Eat and be Healthy, by Lucius Nicholls, C.M.G., M.D., deals with the subjects of diet and nutrition in Ceylon, and contains some useful charts in colour giving the calories and vitamin contents of foodstuffs. It is obtainable from the Associated Newspapers of Ceylon, Langham House, 302 Regent Street, London, W.1, price 4s. 6d. or 5s. 8d. cloth covered.

Enuresis, a memorandum prepared by the Joint Committee of the British Medical Association and the Magistrates' Association on Psychiatry and the Law, deals with the causes and treatment of enuresis in the child and adult. It is published by the British Medical Association, B.M.A. House, Tavistock Square, London, W.C.1.

The contents of the September issue, which will include a symposium on "The Problem of Rheumatism", will be found on page lxxi at the end of the advertisement section.

English medicine was swayed and held in check for three decades by the so-called "theory of focal sepsis". Medical and surgical literature of the 1920's is bespattered with advice to search for and eradicate sepsis as an essential step in the treatment of the most diverse diseases. *Rheumatoid arthritis* was, as it were, the king-pin of the theory. On the flimsiest evidence teeth, tonsils, gall-bladders, sinuses, and colons were subjected to surgical onslaughts. These were followed by two-year courses of vaccine administration. Over a hundred patients a week used to attend hopefully and patiently at one large London hospital alone for their inoculations. Within a year of the introduction of gold treatment the special clinic closed down for lack of support! The French were never bemused by focal sepsis: they leant towards a tuberculous etiology; a theory discarded by us in the last century. In America credit must go to Pemberton, whose voice cried in the wilderness that septic mouths might after all be but a manifestation and not a cause of the disease. The entrenchment of sepsis as a cause of rheumatoid arthritis is understandable because septic arthritis due to known and demonstrable organisms may arise. Furthermore, a form of multiple arthritis, closely resembling the rheumatoid form, called infective or focal arthritis is also known. It is connected with some septic focus, e.g., sore throat, sinusitis or dental abscess. The elimination or subsidence of the focal infection is followed by recovery of the joints. But this disease is a rarity.

In spite of all that has been said to favour a bacterial origin of rheumatoid arthritis it remains a fact that the allegedly causative organisms are not found in blood, urine or joints. It is also true that elimination of foci of sepsis, real and imaginary, does not cure the disease, and the same can certainly be said of vaccines. The lid of the coffin for focal sepsis is decisively nailed down by the recent demonstration that neither sulphonamides nor penicillin exert the least benefit in rheumatoid arthritis. Even the increase of streptococcal agglutinins in this disease has been shown to be due to a non-specific enhancement of the normal feeble agglutinins. We are left with clinical and laboratory evidence favouring an infective agent as the cause of rheumatoid arthritis, and a theory that it may be a virus.

TREATMENT

With two major problems unsolved, it is not surprising that the treatment of rheumatism—the third problem—is in a highly unsatisfactory state. Elimination of sepsis, vaccines, vitamins, endocrines, shock therapy, to mention a few, are in general useless, although occasionally of value as adjuvants. Eradication of focal sepsis and vaccine administration have never cured a case of rheumatoid arthritis. Recently we have been asked seriously to consider the value of alternate withdrawal and injection of spinal fluid, over the course of an hour, in the treatment of rheumatoid arthritis. We have been told also that the joint fluid is abnormally alkaline

for gout, which always searches for an abnormal articulation in which to lay its deposits. Although trauma alone can produce osteoarthritis at any age—and this explains why it complicates the picture of any chronic arthritis—yet advancing years and waning metabolism are its most potent abettors. Thus it is seen so often in both sexes in the sixth and later decades of life. Its frequent occurrence in the hypothyroid post-menopausal woman is too well known to need emphasis. In this form the remarkable regression, and that of the associated villous synovial reaction, after the giving of thyroid is a pointer to the importance of over-weight and failing vitality in etiology.

The intermingling of fact and fantasy in respect of causation is better illustrated in relation to "fibrositis" or *muscular rheumatism* than to any other of this group. Focal sepsis, "metabolic failure", gout, and viruses have all been called in to explain localized or diffuse muscular tenderness and stiffness, with or without the presence of nodules. Even these have been declared to be structureless, composed of a gel, inflammatory masses or local fatty oedema, according to the bias of the investigator. The same signs and symptoms may arise in simple stiff neck following a drive in a car, limbs after unaccustomed exercise, influenza, smallpox, various forms of arthritis, and a host of other diseases. No one etiological factor can possibly account for the many examples which come to mind. It is only a few years since we were told that to break down fibrositic nodules by massage, special percussion hammers, or injections of fluid, was the therapeutic answer to fibrositis.

It is salutary to refer to the work of F. A. Elliot who, in 1944, investigated the tender "fibrositic" nodules in the muscles of the buttock and calf of a series of cases of sciatica. Pressure on them would aggravate the sciatic pain and their injection with procaine would abolish it. Under general anaesthesia the lumps disappeared. Electromyography showed that at the site of the nodules a sustained discharge of action potentials could be demonstrated. Finally, all the cases were subjected to operation for removal of a prolapsed intervertebral disc. The nodules immediately disappeared. In short, they were due to involuntary spasm of small groups of muscle fibres arising from nerve-root irritation.

Such experiments explain one group of "fibrositic" cases and expose the weakness of the theories which attempt to explain all.

Ankylosing spondylitis has provided another fertile ground for the growth of etiological theories. In the early part of this century it was an article of faith that the gonococcus was responsible. It is difficult to understand how such a belief arose, for the proving of such an infection past or present is, in fact, so rare in this disease of young men that, when it does occur, it can be explained on the ground of coincidence. The theory may have been based on the puritanical view that all young men sin, and that the disease is the fruit thereof. No more convincing is the view often expressed here and in America that such spondylitis is a manifestation of rheumatoid arthritis; this in disregard of the fact that the spinal disease is almost exclusively one of young males and never responds to gold treatment. Furthermore, its pathology is quite different.

ment at a spa is of the greatest value in the convalescent stages, as also for gout, osteoarthritis and the more chronic forms of muscular rheumatism. The value of a spa rests in descending order of merit on the quality of its physicians and physiotherapists, the nature of its equipment, the climate, the social amenities of the town, and the nature of its natural waters. In this country the unreliable climate, and the puritanical outlook of successive governments on the lighter but important pleasures of a civilized community, have militated against the popularity which our spas richly deserve. Government supported publicity, and hospitality to foreign physicians, is long overdue. Even in neighbouring countries such as France one is often asked whether there are any spas in England! As the home of rheumatism we deserve something better than this, for we should suffer nothing by comparison with foreign watering-places, and we should gain by the honesty of our claims unvitiated by reference to such fantasies as the curative value of radio-active waters.

RADIOLOGICAL FINDINGS

Perhaps it is here that a word of warning should be uttered against the danger of relying too much upon X-ray pictures for the diagnosis of chronic rheumatism. I have in mind especially the matter of bony irregularity affecting the vertebræ. This "lipping" as it is called is a normal finding in the spines of those over forty years of age. The incidence and prominence of these bony irregularities increase with each further decade. They are a natural reaction to the strains and stresses to which the skeleton is subjected: they are not evidence of osteoarthritis and do not cause symptoms. They must be distinguished from irregular outgrowths of bone, loss of joint space, and changes in bony density which are seen in true osteoarthritis. The warning is necessary because so many middle-aged people with backache are told, because of this lipping, that they have arthritis, and not infrequently that nothing can be done for it.

The second example I have in mind is the statement made by some radiologists that certain circular rarefied areas in bone are typical of gout. There are no X-ray changes produced by gout and gout only. The disease is no more diagnosable by radiology than by biochemical determinations.

Finally, in this respect I urge caution in accepting a statement that an X-ray shows osteoarthritis of the sacro-iliac joints. This is a condition of rarity. The "osteoarthritis" is almost always a normal anatomical variant.

CONCLUSION

If this review is gloomy it should not be disheartening. It should be taken as a warning against the glib exposition of uncontrolled treatments, and as a call for a relentless scientific attack on the scourge of the "rheumatisms". This onslaught is ably furthered by the contributions which follow this article.

and that the disease can be arrested by one or more intra-articular injections of lactic acid! Because the rheumatoid woman usually improves during pregnancy, enthusiasts treat the disease with transfusions of blood taken from a pregnant woman. No thought is given to the fact that pregnancy closely precedes the development of rheumatoid arthritis with great frequency, or that a rheumatoid woman always suffers relapse after pregnancy. It appears to have been forgotten that blood transfusion is in itself often helpful in treatment.

Chrysotherapy.—The only major advance which has been made in the treatment of rheumatism for a century is the introduction of gold therapy. Based on two false premises, namely that the disease of the joints was a manifestation of tuberculosis elsewhere, and that gold was useful in the treatment of tuberculous infection, it has nevertheless brought about a revolution in the treatment of rheumatoid arthritis. Over 80 per cent. of sufferers are restored temporarily to normal and 40 per cent. can be kept well by the intelligent and prolonged use of this empirical therapy. No other treatment can support such claims with the wealth of evidence obtainable for chrysotherapy.

It is probable that the action of gold is an indirect one, attacking the disease through changes it produces in the tissues of the host. It is clearly not a specific, and the strong tendency to relapse shows that the causative agent is not destroyed by the drug. Yet if the patient be treated for two or more years the disease may then disappear, and possibly cure may be established. It is likely that other heavy metals would be similar in their action. The metalloid *bismuth* has been disappointing in comparison with gold.

The *toxic reactions* to gold have frightened many doctors and patients from its use. However, because of a reduction in course-dosage (viz. 0.8 gm.) and the growing use of calcium aurothiomalate, these only occur now in a very small proportion of cases. The severity of the toxic reactions when they occur can now be mitigated by BAL in respect of the skin rash, and pyroxidine to counter agranulocytosis. A patient with rheumatoid arthritis has the right to know that there is at least a four-to-one chance of amelioration of the disease by gold and at most a 10 per cent. risk of troublesome toxic reaction. The only serious reactions I have seen, apart from one case of agranulocytosis, were clearly due to continued administration of gold in spite of warning signs.

The realization that every arthritic joint is an orthopædic problem from the start, and the appreciation of the value and limitations of spa treatment and physiotherapy, emerge also as encouraging advances of the last thirty years. It is now widely recognized that active inflammatory forms of rheumatism, notably rheumatoid arthritis and generalized fibrositis with raised erythrocyte sedimentation rate, are unsuitable at this stage for spa treatment. Such patients are best treated at home. On the other hand treat-

ment at a spa is of the greatest value in the convalescent stages, as also for gout, osteoarthritis and the more chronic forms of muscular rheumatism. The value of a spa rests in descending order of merit on the quality of its physicians and physiotherapists, the nature of its equipment, the climate, the social amenities of the town, and the nature of its natural waters. In this country the unreliable climate, and the puritanical outlook of successive governments on the lighter but important pleasures of a civilized community, have militated against the popularity which our spas richly deserve. Government supported publicity, and hospitality to foreign physicians, is long overdue. Even in neighbouring countries such as France one is often asked whether there are any spas in England! As the home of rheumatism we deserve something better than this, for we should suffer nothing by comparison with foreign watering-places, and we should gain by the honesty of our claims unvitiated by reference to such fantasies as the curative value of radio-active waters.

RADIOLOGICAL FINDINGS

Perhaps it is here that a word of warning should be uttered against the danger of relying too much upon X-ray pictures for the diagnosis of chronic rheumatism. I have in mind especially the matter of bony irregularity affecting the vertebræ. This "lipping" as it is called is a normal finding in the spines of those over forty years of age. The incidence and prominence of these bony irregularities increase with each further decade. They are a natural reaction to the strains and stresses to which the skeleton is subjected: they are not evidence of osteoarthritis and do not cause symptoms. They must be distinguished from irregular outgrowths of bone, loss of joint space, and changes in bony density which are seen in true osteoarthritis. The warning is necessary because so many middle-aged people with backache are told, because of this lipping, that they have arthritis, and not infrequently that nothing can be done for it.

The second example I have in mind is the statement made by some radiologists that certain circular rarefied areas in bone are typical of gout. There are no X-ray changes produced by gout and gout only. The disease is no more diagnosable by radiology than by biochemical determinations.

Finally, in this respect I urge caution in accepting a statement that an X-ray shows osteoarthritis of the sacro-iliac joints. This is a condition of rarity. The "osteoarthritis" is almost always a normal anatomical variant.

CONCLUSION

If this review is gloomy it should not be disheartening. It should be taken as a warning against the glib exposition of uncontrolled treatments, and as a call for a relentless scientific attack on the scourge of the "rheumatisms". This onslaught is ably furthered by the contributions which follow this article.

THE PRESENT STATUS OF GOLD THERAPY IN RHEUMATOID ARTHRITIS

By G. D. KERSLEY, M.D., F.R.C.P.

Physician, Royal National Hospital for Rheumatic Diseases; the Royal United and Orthopaedic Hospitals, Bath; the Bristol Royal Hospital; and to the Arthur Stanley Institute for Rheumatism, Peto Place, London.

WITH the present inadequate knowledge of the fundamental cause of rheumatoid arthritis, no treatment can be considered in any way specific. There is, however, suggestive evidence that at least an important factor in the rheumatoid state is an abnormality in immune body formation (Levinthal, 1939) or antigen-antibody reaction (Wallis, 1947). It is known that the reticulo-endothelial system, the workshop of immunity reactions, has an affinity for gold salts. Stimulation of the reticulo-endothelial system by gold may therefore affect immune body response and hence sensitization, and this may be the mechanism by which aurotherapy benefits a number of cases of rheumatoid arthritis refractory to treatment along more general lines. Although gold salts have been proved to be bactericidal to streptococci and many other organisms *in vitro*, they are less effective in this respect than the sulphonamides, which latter have proved themselves valueless in the clinical treatment of rheumatoid arthritis. It therefore seems fair to assume that the effect of aurotherapy in this disease is not due to a direct action on bacteria. It must be admitted that gold treatment is still empirical, although this does not gainsay its usefulness. In assessing its usefulness, however, the vicissitudes of the disease and its tendency to spontaneous remissions must always be borne in mind, and it is only by examination of carefully controlled work, such as that of Fraser (1945), that any conclusions on its efficacy can be drawn.

The position has recently been well summed up by Hench: "Gold is still extensively used after 20 years of trial and error. The exact value of gold salts in the treatment of rheumatoid arthritis remains uncertain but rheumatologists of experience, with few exceptions, report results therefrom better than those obtained with any other single remedy".

Since the first introduction of aurotherapy in the treatment of rheumatoid arthritis (Lande, 1927; Pick, 1927; Forestier, 1929), views on the subject have gradually crystallized. After a period when high dosage was in use there was a crop of toxic reactions which made many fear to run such risks. Since then, however, less toxic compounds have been discovered, dosage has been decreased, the importance of certain early signs of toxicity have become more widely known, and certain new antidotes have become available. The result has been that it is now agreed by all that the benefits of gold treatment, correctly administered to the correct case, greatly outweigh the risks.

GOLD PREPARATIONS

Many compounds of gold have been tried, but they fall into two main categories, colloid and crystalloid. Sabin (1941) found that the efficacy of gold compounds varied with their gold content, and Tarsy (1940) that colloidal preparations produce a slower clinical improvement and have no bacteriostatic effect on the serum, but produce fewer toxic reactions. According to Freyberg, Block and Levy (1942), colloidal gold, even if given intravenously, disappears from the plasma within thirty minutes, owing to its rapid phagocytosis by the reticulo-endothelial system. The use of these colloidal compounds is now almost obsolete. These workers found, however, that using the crystalline salts by weekly intramuscular injections and working up to a dosage of 50 mgm. of gold by the third week, the plasma content was raised to about 0.8 mgm. per cent. If the dosage was then decreased to 25 mgm. this plasma level fell, even though the excretion did not keep up with the intake. Excretion was mainly in the urine, and gold had in some cases been detected on urinary analysis as long as ten months after the completion of a course. Hartung and Cotter (1940) found a bacteriostatic effect in the serum reaching a maximum when 150 mgm. of gold had been given, this effect disappearing about three months after the last injection.

Either myocrisin (sodium aurothiomalate) or aurocalcium (calcium aurothiomalate) is the preparation most often used in this country, the calcium salt being probably slightly the less toxic. Gold thioglycolanilide (Lauron) is a preparation recently placed on the market, but it seems in no way to be superior to the older and better known preparations (Hench, 1948). An injection of 2 c.cm. of collosol calcium or calcium gluconate at the same time as the gold injection may reduce the tendency to complications, and is in any case a reasonable therapeutic measure.

CLINICAL RESULTS

The value of chrysotherapy has been variously assessed. Price and Leichtenritt (1943) stated that 60 per cent. of patients were markedly improved, but of these, 55 per cent. relapsed, the recrudescences, however, being milder than the original attack. Sundelin (1941), summarizing 3,800 cases quoted in the literature, gave 81 per cent. as markedly improved, whilst L'Orange (1945) found 69 per cent. cured or much improved. The best controlled work on the subject, however, is by Fraser (1945), who in 103 cases found that 82 per cent. of those treated with myocrisin were much improved, as compared with 45 per cent. of the controls.

TOXICITY

There is little doubt that, although toxicity depends to some extent upon idiosyncrasy, the number and gravity of toxic symptoms encountered

increases when the dosage of gold is increased. This impression was borne out by the figures of Price and Leichtentritt (1943), who, giving 50 to 200 mgm. weekly and with courses totalling 0.5 to 4.0 gm., found that 38 per cent. of patients had a moderately severe reaction, particularly when the higher dosage was employed: 25 per cent. developed a dermatitis, and 3 per cent. a severe thrombocytopenia. Hartung and Cotter (1940), giving weekly doses of 50 mgm. subcutaneously, found 15 per cent. had moderately severe toxic symptoms, whereas Freyberg (1942) found no severe reactions with 25 mgm. of the same salt used intramuscularly. Fraser (1945) stated that 75 per cent. of his patients had slight toxic symptoms, but that in only 13 per cent. were they severe enough to make it necessary to discontinue the course. L'Orange (1945), analysing the history of 234 cases, found toxic symptoms in 41 per cent., but in only 2 per cent. were they serious. Sundelin (1941), in his monograph on the subject describing the results of aurotherapy in 730 of his own cases, noted that 58 per cent. of the women and 39 per cent. of the men had some disturbing reaction. Neither age nor duration of the illness seemed to account for this discrepancy. Focal reactions in the joints were not serious, nor was a moderate drop in the white cells or slight albuminuria. In 12 per cent. of his cases there was a toxic, febrile reaction, 45 per cent. showed slight albuminuria, and 17 per cent. had a few red cells in the urine on microscopical examination. An eosinophilia was common (in about 50 per cent. of cases), severe anæmia occurred in 2.6 per cent., severe leucopenia (white cells below 3000) in 3.6 per cent., and a severe thrombocytopenia in 3.1 per cent., a platelet count below 150,000 being an indication that the course of injections should be discontinued, at any rate temporarily. Encephalitic symptoms occurred in 2.3 per cent. In the whole series there were six fatalities: three from thrombocytopenic purpura, two from encephalitis, and one from bronchopneumonia.

Contraindications to chrysotherapy are severe diabetes or nephritis, severe liver damage, any blood dyscrasia, ulcerative colitis, a past history of exfoliative dermatitis, and probably pregnancy. A history of allergy should occasion particular thought before, and care during, gold administration.

To sum up, it seems that severe reactions are rare if one of the less toxic crystalloids is used in small dosage of not more than 50 mgm. at a time, and if it is given intramuscularly at weekly intervals, to a total of not more than 1 gm. per course. A moderate degree of albuminuria without red cells in the urine is not an indication for cessation of treatment. In only about 12 per cent. of cases will it be necessary to cut short the course, the most common cause of annoyance being a dermatitis, which is only occasionally severe. In such cases the patient has the consolation that he is almost invariably cured, at least for a time, of his arthritic symptoms. Again, the use of BAL (British Anti-Lewisite) has greatly reduced the fear of dermatitis (Simpson, 1948): its effect is to inactivate the gold in the

system and will often, within a week, benefit a dermatitis of many months' duration. BAL is given in a 5 per cent. solution in oil with 10 per cent. benzyl benzoate, by deep intramuscular injection. It is usual to start with four injections of 2 c.cm. on the first day, 3 injections for the next three days, and then one daily for the last three days of the course. In a similar way the use of penicillin to control sepsis, should a period of agranulocytosis develop, has also added safety to gold treatment. These two safeguards, together with the use of smaller but more prolonged dosage, have made disasters resulting from aurotherapy relatively rare. Thrombocytopenia is, however, still a dangerous but rare result of gold treatment, although the use of vitamin K may assist in reducing its terrors.

DOSAGE

Dosage must, of course, be regulated according to the patient's reactions: increase in pain in the joints, albuminuria, or slight fever being indications that the dosage should not be increased. If, however, there are no complications the following course may be followed: 0.01 gm. x 3 doses; 0.025 gm. x 3 doses; 0.05 gm. x 18 doses. Total: 1.005 gm.

Within about a month there is often some diminution of pain and swelling, and perhaps an increase in sense of well-being and appetite. If there is any such improvement the course should be repeated in six to twelve weeks. If there is neither clinical improvement nor drop in the sedimentation rate, it is unusual to obtain any benefit from a second course.

Lately from America has come a change in technique with regard to courses of gold. After the first set of injections the gold depot in the body is replenished by less frequent but regular injections maintained for a prolonged period (Freyberg *et al.*, 1942; Cecil, 1946). The interval between injections is gradually lengthened to two, three and then four weeks. This is said to reduce the frequency of relapses after gold therapy. If gold has been discontinued and then another course is indicated, the first injection of the new course should be very small, 0.005 or 0.01 gm., and the dosage gradually built up again to the usual level. Sufficient controlled work on this technique has not yet been published for definite conclusions to be drawn, but the results appear to be encouraging.

ALLERGY

Occasionally a patient may be, or may become, allergic to gold salts even in the smallest dosage. When such a case continues to deteriorate in spite of general treatment, including both physical and psychological rest, good food and physical therapy, resort may be had to the use of other metals or to vaccines in the hope that they will act as satisfactory "alteratives".

S.B.T. (sodium bismuthyl tartrate, 1 grain [65 mgm.] per c.cm.) is sometimes advocated in such cases. It is usual to start with an 0.2 c.cm. dose and then continue with 0.5 c.cm. intramuscularly at monthly intervals

increases when the dosage of gold is increased. This impression was borne out by the figures of Price and Leichtentritt (1943), who, giving 50 to 200 mgm. weekly and with courses totalling 0.5 to 4.0 gm., found that 38 per cent. of patients had a moderately severe reaction, particularly when the higher dosage was employed: 25 per cent. developed a dermatitis, and 3 per cent. a severe thrombocytopenia. Hartung and Cotter (1940), giving weekly doses of 50 mgm. subcutaneously, found 15 per cent. had moderately severe toxic symptoms, whereas Freyberg (1942) found no severe reactions with 25 mgm. of the same salt used intramuscularly. Fraser (1945) stated that 75 per cent. of his patients had slight toxic symptoms, but that in only 13 per cent. were they severe enough to make it necessary to discontinue the course. L'Orange (1945), analysing the history of 234 cases, found toxic symptoms in 41 per cent., but in only 2 per cent. were they serious. Sundelin (1941), in his monograph on the subject describing the results of aurotherapy in 730 of his own cases, noted that 58 per cent. of the women and 39 per cent. of the men had some disturbing reaction. Neither age nor duration of the illness seemed to account for this discrepancy. Focal reactions in the joints were not serious, nor was a moderate drop in the white cells or slight albuminuria. In 12 per cent. of his cases there was a toxic, febrile reaction, 45 per cent. showed slight albuminuria, and 17 per cent. had a few red cells in the urine on microscopical examination. An eosinophilia was common (in about 50 per cent. of cases), severe anæmia occurred in 2.6 per cent., severe leucopenia (white cells below 3000) in 3.6 per cent., and a severe thrombocytopenia in 3.1 per cent., a platelet count below 150,000 being an indication that the course of injections should be discontinued, at any rate temporarily. Encephalitic symptoms occurred in 2.3 per cent. In the whole series there were six fatalities: three from thrombocytopenic purpura, two from encephalitis, and one from bronchopneumonia.

Contraindications to chrysotherapy are severe diabetes or nephritis, severe liver damage, any blood dyscrasia, ulcerative colitis, a past history of exfoliative dermatitis, and probably pregnancy. A history of allergy should occasion particular thought before, and care during, gold administration.

To sum up, it seems that severe reactions are rare if one of the less toxic crystalloids is used in small dosage of not more than 50 mgm. at a time, and if it is given intramuscularly at weekly intervals, to a total of not more than 1 gm. per course. A moderate degree of albuminuria without red cells in the urine is not an indication for cessation of treatment. In only about 12 per cent. of cases will it be necessary to cut short the course, the most common cause of annoyance being a dermatitis, which is only occasionally severe. In such cases the patient has the consolation that he is almost invariably cured, at least for a time, of his arthritic symptoms. Again, the use of BAL (British Anti-Lewisite) has greatly reduced the fear of dermatitis (Simpson, 1948): its effect is to inactivate the gold in the

THE SURGICAL TREATMENT OF RHEUMATOID ARTHRITIS

By W. ALEXANDER LAW, O.B.E., M.D., F.R.C.S.

Assistant Surgeon, Orthopaedic and Accident Department, London Hospital.

MODERN methods of treating the pain, deformities and functional disabilities resulting from rheumatoid arthritis include both conservative and operative procedures. These must not be regarded as isolated phases in the treatment of this condition, but rather as part of a long-term programme in conjunction with medical, physiotherapeutic and, in certain cases, radiotherapeutic measures. Too often in the past, the orthopaedic surgeon has been called in too late to prevent crippling deformity or to have a reasonable chance of restoring function by various joint reconstructions. On the other hand, operative measures are rarely indicated during acute exacerbations of the disease, when judicious immobilization is essential to relieve the muscle spasm and pain, and to prevent increasing deformity. The guiding principles of surgical treatment may therefore be summarized as follows:—

(1) *Relief of pain and arrest of disease.*—This may be achieved by forms of splintage, such as plaster casts, plaster beds and spinal supports, particularly during the acute phases of the disease, and supplementing medical treatment, physiotherapy and, on some occasions, deep X-ray therapy.

(2) *Maintenance and restoration of function.*—In addition to bone rarefaction, muscle atrophy, loss of ligamentous tone and elasticity, peri-articular fibrosis and muscle spasm, together with secondary fasciitis and friction bursitis, are characteristic soft tissue changes which interfere with joint function. It is difficult to restore active movement of rheumatoid joints even by operation if the muscles and ligaments have become reduced to mere strands of fibrous tissue. It is important to maintain muscles in tone and power even during periods of immobilization, and to avoid, if possible, any undue fixation of joints which are not involved. Certain operative procedures are designed to curtail the period of immobilization by relieving pain and allowing active joint function to continue.

(3) *The prevention and correction of deformity.*—During the more acute phases of the disease, this is carried out by immobilization, together with such devices as wedge or turnbuckle plasters, different forms of limb traction and Gatch beds; but once fixed deformity is present it is likely that some type of reconstructive operation will be necessary both to overcome the deformity and restore function. Characteristically there are multiple joint deformities in these cases, and therefore it may be necessary for the patient to be willing to face a long operative programme and to realize that it is essential to give enthusiastic and wholehearted cooperation in the intensive exercise regime that must be carried out for a lengthy period after

for 6 to 12 injections. *Copper salts* are at the moment also under trial for use in this type of case. The dosage at present employed is slightly greater than that used for aurotherapy and toxic reactions have so far been infrequent and not severe. Copper in the form of "alcuprin" (sodium *m*-[N-allylcuprothiocarbamide] benzoate) (May and Baker) has been used with success in a few cases intravenously. The course consists of biweekly injections of 0.1 to 0.25 gm. finishing at a total of 2.5 gm. Another method described by Forestier (1948) is the intramuscular injection of a 10 per cent. solution of cupro-oxyquinoline sulphonate of methylamine, together with 2 c.cm. of 2 per cent. novocain, in biweekly injections of 0.5 gm. to a total of 6 to 9 gm. In 55 cases so treated a slight dermatitis resulted but there were no other complications, even in one who had previously had severe albuminuria with aurotherapy. Too few cases have as yet been observed to allow an opinion to be formed on the degree of benefit likely to accrue.

CONCLUSION

In conclusion, it is fair to state that any case of rheumatoid arthritis, which has a rapid sedimentation rate, and which is not definitely improving after a month of so of rest, both mental and physical, coupled with good food, analgesics, and elimination of definite sepsis, should be given the benefit of gold therapy. If, during the course of treatment, a watch is kept on the skin and the urine, and periodic platelet and white counts are done, then the risk of severe toxic symptoms is slight and is far outweighed by the likely therapeutic advantages.

References

- Cecil, R. L. (1946): *Med. Clin. N. Amer.*, **30**, 545.
 Forestier, J. (1929): *Bull. Mém. Soc. méd. Hôp Paris*, **1**, 323.
 —, Jacqueline, F., and Lenoir, S. (1948): *Presse méd.*, **56**, 351.
 Fraser, T. N. (1945): *Ann. rheum. Dis.*, **4**, 71.
 Freyberg, R. H. (1942): *Ibid.*, **3**, 77.
 —, et al. (1942): *Clinics*, **1**, 537.
 Hartung, F., and Cotter, J. (1940): *J. Lab. clin. Med.*, **26**, 1274.
 Hench, P. S., et al. (1948): *Ann. intern. Med.*, **28**, 1.
 Lande, K. (1927): *Munch. med. Wschr.*, **74**, 1132.
 L'Orange, W. (1945): *Saertrykk Nod. Med.*, **26**, 893.
 Levinthal, W. (1939): *Ann. rheum. Dis.*, **1**, 67.
 Pick, E. (1927): *Munch. med. Wschr.*, **40**, 1175.
 Price, A. E., and Leichtentritt, B. (1943): *Ann. intern. Med.*, **19**, 70.
 Sabin, A. B. (1941): *Bact. Rev.*, **5**, 1.
 Simpson, N. R. W. (1948): *Brit. med. J.*, **1**, 545.
 Sundelin, F. (1941): *Acta med. Scand.*, suppl. 117.
 Tarsy, J. M. (1940): *J. Lab. clin. Med.*, **26**, 1918.
 Wallis, A. D. (1947): *Ann. rheum. Dis.*, **6**, 86.

with fascia, but this is not essential if an adequate amount of bone has been removed from the humerus, radius and ulna. A more stable, although less freely movable joint can be obtained by performing the arthroplasty in such a way that the lower end of the humerus and the upper end of the ulna are reshaped so as to articulate freely with one another, the head of the radius and synovial membrane being excised.

In the shoulder joint, pain and adduction internal rotation deformity are commonly associated with severe muscle spasm, subacromial bursitis and periarthrititis. The thickened and inflamed bursa is productive of much pain and the accompanying muscle spasm restricts both gleno-humeral and scapulo-thoracic movements.

Excision of the acromion process, through the acromio-clavicular joint, together with the villous synovial membrane of the underlying bursa, removes the main focus of pain and allows the central tendon of the deltoid to glide freely over the shoulder-cuff, which can also be examined and reconstructed if necessary. Residual abductor weakness is avoided by suturing the deltoid to the periosteal attachment of the trapezius. If there is marked destruction of the gleno-humeral joint and the scapular muscles are functioning, pain and disability are overcome by arthrodesing the shoulder joint in about fifty degrees of abduction with slight forward flexion and external rotation. Such a position enables the patient to carry the arm to the side and, by virtue of moving the scapula, there is sufficient painless abduction for useful function.

It should be noted that in rheumatoid arthritis involving the upper extremities, apart from arthroplasty of the elbow and arthrodesis of the shoulder or wrist, there are several relatively simple operations which are of considerable value in relieving pain and maintaining function. These operations should therefore be employed before the disease process and the accompanying muscle spasm have produced fixed deformity and distorted or ankylosed the joints. With the maintenance of function, muscle tone and power can be restored, at least partially, and this is of great importance should more major reconstructions be required at a later date.

LOWER LIMB PROCEDURES

In the lower extremities surgical treatment must not interfere with stability in weight bearing which is an all-important function. Joint reconstruction must provide painless and stable joints, and these criteria should not be sacrificed merely to provide movement.

As in the hand, the *small joints of the feet* are often involved, with resultant painful claw-toe deformities and dropping of the metatarsal heads. Subluxation of the metatarso-phalangeal joints may also occur together with hallux valgus deformity and soft tissue changes, such as adventitious bursæ and painful callosities. Spike arthrodesis of the interphalangeal joints effectively controls the hammer-toe deformity, and resection of the metatarsal heads in the second, third and fourth toes alleviates the effects of subluxation. The footwear is fitted with domed insoles to support the metatarsal arch and enable correct weight bearing on the heads of the first and fifth metatarsals. Hallux valgus deformity is best treated by the Kellar operation, making certain that the base of the proximal phalanx is adequately

all the operations that are designed to restore function. It may be necessary, in addition, to have operative revisions in order to obtain satisfactory end-results.

Before embarking upon operative treatment it is essential that there should be no foci of infection or any anaemia, and to diminish the risk of infection by penicillin control.

UPPER LIMB PROCEDURES

The hands and wrists are commonly involved in rheumatoid arthritis, with pain and swelling in the joints and ultimately flexion and ulnar deviation deformity. Loss of movement may also be associated with subluxation at the interphalangeal and metacarpo-phalangeal joints. Capsulotomy or capsulectomy may help in restoring function, but usually must be combined with resection of adjacent bone ends in the interphalangeal joints or of the metacarpal heads in the metacarpo-phalangeal joints. Fascia lata may be used as an interposition membrane to prevent re-ankylosis and, in the case of the thumb, Smith-Petersen has devised a vitallium mould for the same purpose. Careful postoperative supervision is essential to obtain satisfactory function of a type in which power is sacrificed for diminution of pain, at least partial correction of deformity and restoration of movement.

The function of the hand is materially affected by wrist joint pain and deformity, and inferior radio-ulnar arthritis. In the latter case, pain can be relieved and rotation restored simply by excising the lower end of the ulna. When the radio-carpal joint is also involved, this is combined with arthrodesis of that joint in the position of maximal function—about twenty degrees of dorsiflexion. The whole operation is performed through the approach over the lower end of the ulna, which itself is used as a graft in the radio-carpal arthrodesis.

The hand and wrist joint function may also be further impeded if *the elbow joint* is involved. Smith-Petersen *et al.* (1943) and Law (1948) have drawn attention to the fact that severe and persistent spasm of the biceps muscle may draw the head of the radius up so forcibly that a joint defect is produced in the articular surface of the capitellum. Excision of the head of the radius, together with subtotal synovectomy of the elbow joint, relieves pain and muscle spasm with consequent improvement, particularly in the range of pronation and wrist joint function, as well as a lesser improvement in elbow flexion and extension. This operation should be performed relatively early in the disease, before there is extensive elbow joint disintegration and the likelihood of complete ankylosis, which demand treatment by formal arthroplasty.

In rheumatoid arthritis, owing to the fibrosis in the periarticular tissues, the best type of arthroplasty is that in which the elbow joint is excised at the levels of the neck of the radius distally and the supracondylar region proximally. This does not result in an excessively flail joint, and relieves pain and deformity in addition to restoring a useful range of flexion and extension. The raw bone ends may be covered

with fascia, but this is not essential if an adequate amount of bone has been removed from the humerus, radius and ulna. A more stable, although less freely movable joint can be obtained by performing the arthroplasty in such a way that the lower end of the humerus and the upper end of the ulna are reshaped so as to articulate freely with one another, the head of the radius and synovial membrane being excised.

In the shoulder joint, pain and adduction internal rotation deformity are commonly associated with severe muscle spasm, subacromial bursitis and peri arthritis. The thickened and inflamed bursa is productive of much pain and the accompanying muscle spasm restricts both gleno-humeral and scapulo-thoracic movements.

Excision of the acromion process, through the acromio-clavicular joint, together with the villous synovial membrane of the underlying bursa, removes the main focus of pain and allows the central tendon of the deltoid to glide freely over the shoulder-cuff, which can also be examined and reconstructed if necessary. Residual abductor weakness is avoided by suturing the deltoid to the periosteal attachment of the trapezius. If there is marked destruction of the gleno-humeral joint and the scapular muscles are functioning, pain and disability are overcome by arthrodesis the shoulder joint in about fifty degrees of abduction with slight forward flexion and external rotation. Such a position enables the patient to carry the arm to the side and, by virtue of moving the scapula, there is sufficient painless abduction for useful function.

It should be noted that in rheumatoid arthritis involving the upper extremities, apart from arthroplasty of the elbow and arthrodesis of the shoulder or wrist, there are several relatively simple operations which are of considerable value in relieving pain and maintaining function. These operations should therefore be employed before the disease process and the accompanying muscle spasm have produced fixed deformity and distorted or ankylosed the joints. With the maintenance of function, muscle tone and power can be restored, at least partially, and this is of great importance should more major reconstructions be required at a later date.

LOWER LIMB PROCEDURES

In the lower extremities surgical treatment must not interfere with stability in weight bearing which is an all-important function. Joint reconstruction must provide painless and stable joints, and these criteria should not be sacrificed merely to provide movement.

As in the hand, the small joints of the feet are often involved, with resultant painful claw-toe deformities and dropping of the metatarsal heads. Subluxation of the metatarso-phalangeal joints may also occur together with hallux valgus deformity and soft tissue changes, such as adventitious bursæ and painful callosities. Spike arthrodesis of the interphalangeal joints effectively controls the hammer-toe deformity, and resection of the metatarsal heads in the second, third and fourth toes alleviates the effects of subluxation. The footwear is fitted with domed insoles to support the metatarsal arch and enable correct weight bearing on the heads of the first and fifth metatarsals. Hallux valgus deformity is best treated by the Kellar operation, making certain that the base of the proximal phalanx is adequately

resected, and that a postoperative regime, including intrinsic foot exercises and maintenance of the toe re-alignment by strapping, is carried out with due care.

Pain, persistent swelling and deformity in the mid-tarsal or ankle joints are best treated by triple arthrodeses or fusion of the ankle joint, respectively, resections of the bone being carried out when necessary to render the foot plantigrade for purposes of walking. By such means, even in the common cases of bilateral rheumatoid involvement, gait can be made painless and stable, without loss of balance or undue stress and strain on the larger and more proximal joints.

The knee joint presents a great problem in treatment. Flexion deformity may be held in check by plaster casts, or even overcome by wedge plasters or turn-buckle devices and traction, but a painful unsound fibrous ankylosis is likely to occur. In some cases there is a "joint-cycle", with pain, gross effusion, resolution and a quiescent period in almost regular rotation. Such cases respond well to joint aspiration, followed by a pressure bandage and graduated mobilization. If there is incomplete resolution between the acute exacerbations, and the synovial membrane undergoes villous hypertrophy, the recurrent effusion and the tendency to flexion deformity can be overcome by subtotal excision of the synovial membrane, together with the internal and external menisci and protuberant fatty pad, thus increasing the joint space. In the more severe cases, and those with a slight degree of joint subluxation, posterior capsulotomy and division of the posterior cruciate and even the lateral ligaments, enable the deformity to be corrected and some movement to be maintained. Forceful correction should be avoided owing to the danger of overstretching the tibial and peroneal nerves or injuring the popliteal vessels, and it is easier and safer to strip the posterior capsule subperiosteally, lengthening the hamstring tendons if necessary. When the joint surfaces have been disintegrated by the rheumatoid pannus, arthrodesis or arthroplasty are indicated. The former assures painless stability, although bilateral stiff knee joints are inconvenient; particularly when sitting. The latter procedure is still uncertain both as regards relief of pain and the amount of movement regained. Vitallium plates have been introduced by Smith-Petersen in America and Thrapp-Mayer in Norway in an effort to prevent re-ankylosis, and some success has been obtained by reshaping the lower end of the femur into single or double condyles to articulate with corresponding congruous surfaces reformed on the upper end of the tibia, lining the new articular surfaces with fascia lata, although this is by no means essential.

In my own experience so far, sound arthrodesis provides better function. This is readily achieved by resecting the synovial membrane and articular cartilage from femur, tibia and patella, and inserting a short three-flanged Smith-Petersen nail obliquely across the coapted bone surfaces, which are also packed with cancellous bone chips. In bilateral cases the operation on

the second side may be performed within two or three weeks or it may be deferred until the functional result of unilateral arthrodesis has been determined.

THE HIP JOINTS

In the case of the hip joints, where again bilateral involvement is likely, the choice of operative reconstruction lies between some form of arthroplasty or pseudarthrosis. In some cases the latter procedure may provide a wider range of movement, but unless stability is adequately retained, subsequent weight bearing will not be satisfactory. The various forms of arthroplasty using such interposition membranes as fascia lata or pig's bladder usually merely result in re-ankylosis. A great advance has been made by Smith-Petersen (1948) using an accurately shaped vitallium mould or cup, which is quite inert in its reactions with the tissue fluids and enables new joint surfaces made of fibro-cartilage with a hyaline appearance, capsule, synovial membrane and synovial fluid to be re-formed by organization of the surrounding blood clot, according to the principle of Wolff's law, structure being adapted to function. The prospects of success with this type of operation depend upon several important factors:—

(1) The decision to pursue such treatment before muscle wasting and periarticular fibrosis are extreme.

(2) The availability of special instruments and intimate knowledge of the operative technique, which is somewhat specialized.

(3) The willingness on the part of the patient to carry out an intensive exercise regime after operation, over a period of at least two years. The operations are useless without this cooperation, and the surgeon himself must be prepared to supervise this rehabilitation in detail.

(4) The realization that in order to obtain good function finally, it may be necessary to perform further operative revisions in order to correct such defects as faulty relationship of the mould, excessive new bone formation, the use of too small a mould, or too shallow and too small an acetabulum, with fibrous or bony ankylosis. These revisions are designed to increase the range of movement and the power of the muscles.

There are four types of *vitallium mould arthroplasty* to consider. They all involve the same principles of excising the joint capsule and rheumatoid pannus, accurately reshaping smooth and congruous surfaces on the femoral head and acetabulum at the level of healthy bleeding bone, the acetabulum being made large and deep. The cup which is inserted must be freely movable both on the upper end of the femur and in the acetabulum, yet remaining perfectly stable.

(1) The routine arthroplasty, in which new joint surfaces are made between the femoral head and the acetabulum, and the vitallium mould fitted accordingly.

(2) The modified Whitman operation, which is indicated when bone atrophy necessitates sacrificing the femoral head. The femoral neck is made congruous with the acetabulum, and the mould is placed on the proximal end of the neck. The greater trochanter with its attached muscles is transposed down the femoral

shaft in order to lengthen the neck, and this may be carried out as a primary or secondary procedure.

(3) The modified Colonna operation is required in cases in which both the femoral head and neck are atrophied or absorbed. The muscles are freed from their attachments to the trochanter, which is made congruous with the acetabulum and fitted with a mould, obtaining as much varus relationship as possible.

(4) The intertrochanteric or proximal shaft arthroplasty. This is the same type of procedure performed more distally on the femur and indicated when the greater trochanter is unsuitable for reshaping.

In order to improve the stability in the last two operations, it is often necessary to deepen the acetabulum by a vertical osteotomy of the roof margin, opening up a gap laterally and packing this with cancellous bone chips from the iliac crest. Ideally, the operations on the two sides are performed two or three weeks apart so as to utilize the same rehabilitation period, but care must be taken that the patient's general condition, particularly a hæmoglobin level near 100 per cent., allows two such major operations at this short interval.

The *postoperative regime* includes suspending the limb in light balanced traction for four weeks, during which time active exercises and assisted movements are instituted. This is followed by mobilization in bed for two weeks and the beginning of abduction and adduction exercises with skates strapped on to the back of the heels, working on a hinged board. After the sixth week the patient is allowed up, rapidly progressing from sitting to the use of crutches, and being instructed carefully in a correct heel-toe, high-stepping gait from the outset. The new hip joints are protected by the use of crutches for at least three months, and as the muscle power and stability improve they are replaced by walking sticks. It should be noted that this line of treatment does not entail plaster immobilization with the danger of restricting movement in adjacent joints, nor, on account of instability, are walking calipers required during the early ambulatory phase.

Excision of the head and neck of the femur (Girdlestone, 1945), and this combined with abduction osteotomy at the subtrochanteric level (Batchelor, 1945; Stamm, 1942), are pseudarthroses designed for restoring hip movement with relief of pain, but in my opinion stability is less easily obtained. In addition there is considerable loss of leg length, although this applies also to the modified Colonna and proximal shaft arthroplasties and is of less significance in bilateral cases. In these latter types of arthroplasty, there is a similar amount of bone resection, but an effort is made to re-establish a stable and painless joint by making congruous joint surfaces in addition to providing a useful range of movement.

THE SPINE

Severe *rigid kyphosis* of the dorsal spine is a common deformity in ankylosing spondylitis, but is less frequently seen as the result of rheumatoid arthritis. The deformity can also be exaggerated by permanent flexion deformity of the hip joints and the inability to form a compensatory lumbar lordosis owing to ankylosis of that region of the spine.

Spinal osteotomy.—In order to enable these patients to resume a more or less upright position and to be able to look ahead, Smith-Petersen (1945) devised the operation of spinal osteotomy.

Wedges of bone are excised from the intra-articular facets, together with bone in the ligamenta flava at one or more levels in the lumbar spine. The spine is then hyperextended so as to close the gap, without compressing the spinal cord or overstretching the important anterior soft structures such as the femoral and autonomic nerves or larger vessels. After an adequate lumbar lordosis has been obtained to compensate for the dorsal kyphosis, spinal fusion is carried out to complete the operation, and further immobilization is required until there is bony consolidation.

A similar operation may be performed with greater technical difficulty in the dorsal region, but as a rule adequate correction can be obtained by lumbar spinal osteotomy, particularly if a severe hip flexion deformity has previously been corrected by arthroplasties. This operation is one which requires skill, time and patience to execute, but the results are excellent. Any tendency for the spine to slump during the early postoperative period is controlled by wearing a long spinal brace for the first year while the spinal muscles are being redeveloped by an intensive course of exercises. Care must be taken to avoid overcorrection, as in such circumstances the patient will not be able to see his feet or carry out acts close to his body under direct vision, and in severe cases it may be necessary to complete the correction in two or more stages.

THE JAW

It is not uncommon for the temporo-mandibular joints to be involved, with pain and inability to open the jaws. Arthroplasty of these joints by resection of the condyles of the mandible, overcomes this problem effectively, although in the early stages after the operation on the second side, care must be taken to avoid recession of the mandible and aspiration of the tongue during sleep. This operation may be a necessary preliminary for further procedures requiring intubation anaesthesia.

CONCLUSION

Surgical treatment in rheumatoid arthritis is carried out only in conjunction with all other forms of therapy. Its great value and object is restoration of at least partial function free from pain, thereby enabling bedridden and deformed invalids to become ambulant and even to resume certain occupations. In this way a great deal may be achieved for the patients' morale as well as for their physical well-being.

References

- Batchelor, J. S. (1945): *Proc. Roy. Soc. Med.*, 38, 12, 685.
 Girdlestone, G. R. (1945): *Ibid.*, 38, 7, 363.
 Law, W. A. (1948): *Ibid.*, 41, 251.
 — (1948): *J. Bone Jt. Surg.*, 30 B, 76.
 Smith-Petersen, M. N. (1948): *Ibid.*, 30 B, 59.
 —, Aufranc, O. E., and Larson, C. B. (1943): *Arch. Surg.*, 46, 764.
 —, —, — (1945): *J. Bone Jt. Surg.*, 27, 1.
 Stamm, T. T. (1942): *Proc. Roy. Soc. Med.*, 35, 221.

SOME INDUSTRIAL ASPECTS OF RHEUMATISM

By THOMAS FERGUSON, M.D., D.Sc., F.R.C.P.Ed., F.R.F.P.S.G., F.R.S.E.

Professor of Public Health, University of Glasgow.

WHEN Sir John Sinclair prepared his famous "Statistical Account of Scotland" at the end of the eighteenth century he reported that rheumatism, but little known at the beginning of the century, was very prevalent: "There is not a Parish in Scotland, in which it is not now very generally felt". Several factors were held to be responsible for this increased prevalence of rheumatism—the climate, the miserable nature of the houses, the clothing of the people, and their increasing pursuit of a sedentary mode of life. Sinclair's analysis of the occupations of the people showed that whilst at the end of the century the largest individual group of occupations was still that associated with agriculture, an ever increasing number were coming to be employed in manufactures of various kinds, in building, and on work in mines and quarries. A little later (1845) the second Statistical Account, describing a reconstructed cotton mill at Deanston, in Perthshire, commended the introduction of a new type of factory flooring, a thin covering of wood over solid stone: "The floor so arranged affords the solidity of a stone floor, and the advantages of the wooden surface to the workers are a diminution of swelled ankles and rheumatic affections of the joints, often produced by working bare-footed on stone floors".

Sinclair recognized the great social and economic importance of rheumatism: "There is no subject [he wrote] to which the real philanthropist can direct his attention with a greater prospect of doing good than by endeavouring to alleviate the distresses which rheumatism occasions among so many thousands of his fellow subjects; for it almost universally renders the decline of life a state of increasing misery". As was to be expected, innumerable recipes for the cure of rheumatism have been recommended, and Sinclair gave details of a cure which he regarded as among the simplest and best: "One ounce and a half best sulphur, one ounce best calcined magnesia; to be put in an English quart or a Scotch chopin bottle and filled up with whisky: take a wineglassful morning and night, shaking it well before taken".

VARIATIONS IN INCIDENCE WITH OCCUPATION AND WITH AGE

Variations in incidence of rheumatism with the nature of occupation have long been known. In the Annual Report of the Department of Health for Scotland on "Incapacitating Sickness among the Insured Population of Scotland", published in 1935, it was shown that the incidence of incapacity

from rheumatic and joint conditions among miners in Scotland was more than twice as high as among other insured males, whereas the figures for workers in agriculture was below the average figure. In 1945, in an Appendix to the "Report on Chronic Rheumatic Diseases", the Department produced figures for the incidence of rheumatism in selected occupational groups, and from these tables the following figures have been extracted:—

TABLE 1

RHEUMATISM: SCOTTISH INSURED POPULATION (MALES), 1937-38. INCAPACITY RATE PER 1000 WORKERS IN EACH OCCUPATIONAL GROUP

Occupational group	Type of Rheumatism				Total Rheumatism
	Muscular	Neuritic	Chronic articular	Acute	
Mining	38.27	6.77	2.37	0.69	48.10
General labouring ..	27.49	4.43	1.99	0.31	34.42
Metal	19.85	3.36	1.52	0.58	25.31
Agriculture and fishing	17.05	3.15	1.72	0.53	22.45
Domestic	12.22	2.16	1.59	0.72	16.69
Commercial	11.62	2.21	1.08	0.65	15.56
All males	20.94	3.66	1.70	0.60	26.90

From these figures it appears that the incidence of muscular rheumatism runs roughly parallel to that of the neuritic type; chronic joint rheumatism shows the same trend, although to a lesser extent, whilst acute rheumatism does not show such wide fluctuations with occupational group. The total number of new incapacities from rheumatism arising among the Scottish insured population during the year 1937-38 was over forty-five thousand (from an insured population of 1,837,000), and the burden of rheumatism was markedly heavier in the central industrial belt than in other parts of

TABLE 2

RHEUMATIC DISEASES AMONG THE SCOTTISH INSURED POPULATION 1933-36. INCIDENCE RATES PER 1000 FOR AGE AND SEX

Age-group	Type of Rheumatism					
	Muscular group		Neuritic group		Articular group	
	M	F	M	F	M	F
15-19	8.6	10.5	0.5	0.7	2.6	3.3
20-24	11.9	13.8	1.1	1.5	3.4	3.5
25-29	15.8	13.8	2.0	2.5	3.7	2.9
30-34	22.6	14.9	3.3	3.0	3.5	3.3
35-39	24.6	17.1	4.1	3.6	3.5	3.1
40-44	25.2	20.2	4.9	4.8	3.5	3.8
45-49	27.4	23.8	5.7	5.2	3.6	5.1
50-54	28.9	24.1	6.2	5.7	3.8	5.3
55-59	30.6	22.7	6.8	5.8	4.4	5.7
60 and over	33.4	24.4	8.1	5.8	5.6	7.5
All ages	20.8	15.1	3.6	2.5	3.6	3.7

the country. Incidence rates increased strikingly with age, and this variation with age was even greater for rheumatism than for incapacitating sickness generally.

It will be observed (table 2) that the influence of age is less marked in articular rheumatism than in the neuritic and muscular forms of the disease, and that the excess of male cases in the muscular and neuritic groups does not hold for articular cases. Sutherland and Whitwell (1948) have confirmed the importance of rheumatic disease as a contributor to incapacity for work in different types of engineering factories.

Recently, in the course of a survey of hospital-treated sickness of all kinds among the population of a typical Scottish county, information was obtained about the number of cases of rheumatism treated and of certain possibly associated conditions. The total number of cases of rheumatism covered by the survey was not large and, particularly for acute rheumatism, too small to permit of comparison of one industrial group with another; but the incidence of cases of chronic rheumatic disease treated was notably high among the metal workers, who bulked so large in the industrial community concerned (table 3).

TABLE 3
OCCURRENCE OF CERTAIN TYPES OF HOSPITAL-TREATED SICKNESS IN A MIXED COUNTY
POPULATION: STIRLINGSHERE, 1946-47

Condition	Miners		Metal workers		All males over 15 years of age	
	I.P.	O.P.	I.P.	O.P.	I.P.	O.P.
Acute rheumatic fever	3	—	1	1	10	3
Fibrositis, muscular rheumatism, including lumbago	1	18	—	37	6	140
Arthritis, all forms	3	12	7	30	31	132
Diseases of ligaments	—	4	1	7	3	31
Internal derangement of knee joint ..	14	3	2	6	23	29
Bursitis, synovitis	9	9	0	10	13	49
Sprains, strains	5	59	5	100	18	475
Approximate population involved ..	7000		9,300		65,500	

I.P. = In-patient.

O.P. = Out-patient.

The occurrence of sprains and strains, as that of chronic rheumatism, was above average in the group of metal workers, and the excess was of a similar order. Bursitis and synovitis were found to call for treatment more frequently among coal miners, which accords with the known prevalence of these conditions in that industrial group. Whether the high prevalence of internal derangement of the knee joint among miners is to be regarded as occupational, or merely as an expression of the enthusiasm of young miners for playing football, is still uncertain.

RHEUMATISM AND INDUSTRIAL TRAUMA

It is notoriously difficult to differentiate between rheumatism and some of

the less spectacular late results of trauma. In industrial disabilities the differentiation may sometimes be wellnigh impossible; there can be no doubt that rheumatism among industrial workers is often a direct expression of the late effects of injury, or repeated minor injuries, or even, perhaps, of the habitual overaction of a particular group of muscles. This is well demonstrated in the frequent complaints of low back pain associated with work involving heavy lifting, as, for instance, the back pain of miners and of iron moulders. My colleague, Dr. John Rogan, reporting on a series of cases of back pain in iron moulders, found that the condition was commonly one of myo-ligamentous strain, and the workmen concerned often gave a history of wrenching associated with repeated lifting or the execution of other movements involved in moulding. The onset of back pain in such employments is probably especially liable to occur where there is some pre-existing abnormality of the back. It is well known in moulding districts that tall workers are more prone to develop backache than are short workers, and it is common enough to hear it said of a youngster about to enter industry that he is "too long in the back" to make a moulder; apparently the ideal recruit to moulding should be of anthropoid type, with short back and long arms. It is worth noting that in many of these cases of "rheumatism", although the cause of the trouble is chiefly myo-ligamentous, there is also present a measure of osteoarthritic change, sometimes advanced, particularly in older workers; and that the occupational groups associated with high incidence of chronic rheumatism are, in general, those which also carry a high proportion of injuries.

Many have learned that "lumbago" is apt to overtake the zealous gardener at the beginning of his season's digging. Sir Harold Stiles used to bracket in this connexion the unwonted digging and the consumption of new season's rhubarb. A considerable amount of similar muscular discomfort, though of less compelling severity, often follows the repeated execution of movements not in themselves calling for the expenditure of much muscular exertion, especially when these movements are carried out under faulty postural conditions. As examples may be cited the discomfort in the back between the scapulæ that comes of typing when seated on a chair that is too low, or the same type of pain, in much the same position and probably associated with faulty posture of the shoulder girdle, that comes of much knitting, especially among those who are not fluent knitters; a condition that our grandmothers sought to mitigate by wearing a device which supported their knitting-needles at a suitable level. The same type of discomfort in the upper scapular region is often experienced by motorists when the driving seat is too low relative to the steering wheel; this kind of discomfort, like that of typists mentioned above, can be relieved simply enough by raising the level of the seat.

Occupational factors involved.—Among the occupational factors generally accepted as major contributors to rheumatism are abnormal working

the country. Incidence rates increased strikingly with age, and this variation with age was even greater for rheumatism than for incapacitating sickness generally.

It will be observed (table 2) that the influence of age is less marked in articular rheumatism than in the neuritic and muscular forms of the disease, and that the excess of male cases in the muscular and neuritic groups does not hold for articular cases. Sutherland and Whitwell (1948) have confirmed the importance of rheumatic disease as a contributor to incapacity for work in different types of engineering factories.

Recently, in the course of a survey of hospital-treated sickness of all kinds among the population of a typical Scottish county, information was obtained about the number of cases of rheumatism treated and of certain possibly associated conditions. The total number of cases of rheumatism covered by the survey was not large and, particularly for acute rheumatism, too small to permit of comparison of one industrial group with another; but the incidence of cases of chronic rheumatic disease treated was notably high among the metal workers, who bulked so large in the industrial community concerned (table 3).

TABLE 3
OCCURRENCE OF CERTAIN TYPES OF HOSPITAL-TREATED SICKNESS IN A MIXED COUNTY
POPULATION: STIRLINGSHIRE, 1946-47

Condition	Miners		Metal workers		All males over 15 years of age	
	I.P.	O.P.	I.P.	O.P.	I.P.	O.P.
Acute rheumatic fever	3	—	1	1	10	3
Fibrositis, muscular rheumatism, including lumbago	1	18	—	37	6	140
Arthritis, all forms	3	12	7	30	31	132
Diseases of ligaments	—	4	1	7	3	31
Internal derangement of knee joint ..	14	3	2	6	23	29
Bursitis, synovitis	9	9	0	10	13	49
Sprains, strains	5	59	5	100	18	475
Approximate population involved ..	7000		9,300		65,500	

I.P. = In-patient.

O.P. = Out-patient.

The occurrence of sprains and strains, as that of chronic rheumatism, was above average in the group of metal workers, and the excess was of a similar order. Bursitis and synovitis were found to call for treatment more frequently among coal miners, which accords with the known prevalence of these conditions in that industrial group. Whether the high prevalence of internal derangement of the knee joint among miners is to be regarded as occupational, or merely as an expression of the enthusiasm of young miners for playing football, is still uncertain.

RHEUMATISM AND INDUSTRIAL TRAUMA

It is notoriously difficult to differentiate between rheumatism and some of

to enable him to utilize as much as possible of his trade skill. A minority is so severely handicapped as to be quite incapable of work under ordinary industrial conditions, and for them some form of sheltered employment may be necessary: experience has shown that, given careful selection of product, it is possible to employ on an economic basis even severely disabled people under sheltered workshop conditions, provided care is taken to build up a reasonably balanced team, and provided a certain proportion of the workers—perhaps up to 20 per cent.—have sufficient freedom of action to keep the manufacturing process moving.

ACUTE RHEUMATISM

As already indicated, acute rheumatism, unlike the more chronic forms of the disease, is not a major contributor to incapacity for work among the insured population, nor does it fluctuate with occupational group to the same extent as the other. But acute rheumatism is, none the less, of considerable industrial importance, and not nearly enough attention is given to skilled vocational guidance designed to see that the young person with a history of acute rheumatism seeking to enter industry is, from the first, trained for work consistent with his capacity. It too often happens that young people with gross rheumatic heart disease are allowed to drift into work involving heavy physical demands which can only lead to early breakdown. In this connexion it is worth recalling that some employments eminently suited to the physical and mental capacities of these youngsters are more or less closed to them by the operation of superannuation schemes, sufficiently drastic in their pre-employment requirements to exclude potential workers with rheumatic heart disease from employment of a kind most likely to afford them success and happiness in life.

References

- Department of Health for Scotland (1935): "Annual Report on Incapacitating Sickness among the Insured Population," p. 42.
 Department of Health for Scotland (1945): "Report on Chronic Rheumatic Diseases," appendix.
 Glasgow Bureau of Health and Sickness Records (1948): "Hospital and Community," p. 83.
 Sinclair, John (1825): "Statistical Account of Scotland," Part 1, p. 131.
 Sutherland, Ian, and Whitwell, G. P. B. (1948): *Brit. J. indust. Med.*, 5, 77.

postures; violent exertion; the over-use of certain muscle groups and joints; and rapid changes or extremes of temperature, damp and wet. These conditions are to be found chiefly in the heavy industries, and it is therefore not surprising that the heavy industries yield more than their quota of chronic rheumatism; this excess is most marked in the muscular and neuritic forms of the disease.

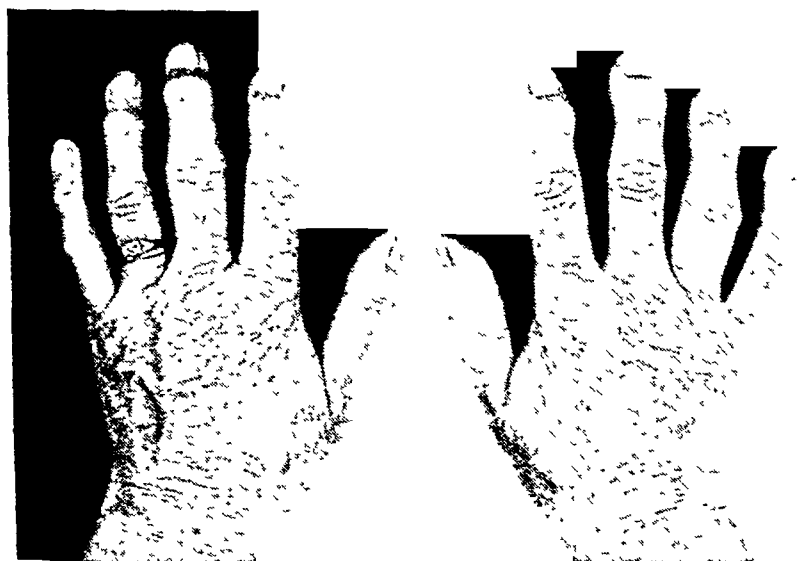
The need for intensive research on the industrial aspects of rheumatism has often been stressed: "need for the coordination of research in industrial medicine with the investigation of the clinician and the laboratory worker on rheumatism", as the report on Chronic Rheumatic Diseases of the Department of Health for Scotland had it. One of the first essentials in any effective research of the kind must be the provision of facilities for accurate diagnosis, and, armed with these facilities, a survey of industrial processes in the industries in which the incidence of rheumatism is high, to ascertain the relevant working conditions as a basis for remedial action. It is gratifying to learn that the National Coal Board and the Department of Industrial Health in the University of Manchester are about to cooperate in a research of this kind.

THE NEED FOR EXPANSION OF TREATMENT FACILITIES

If the amount of invalidism from rheumatism is to be reduced, there must be an expansion of treatment facilities in industrial centres, with, in particular, the provision of treatment facilities available at times which permit of their use by workpeople without encroachment on working shifts. The centres in which treatment can be obtained for chronic rheumatic conditions in the evenings are not nearly so numerous as they ought to be. Pressure on limited existing facilities for physiotherapy is so great that it is often difficult for the industrial worker to secure treatment directed to the relief of pain, especially in cases in which spectacular cure is no longer possible. Some physiotherapists, hard pressed for time, are reluctant to deal with these cases; yet facilities for the relief of pain may make all the difference between capacity for work and enforced idleness.

Some 4 per cent. of the 900,000 (or thereby) persons registered as disabled under the Disabled Persons (Employment) Act suffer from arthritic or rheumatic disease: many of them are able to continue at work more or less similar to that to which they have been accustomed, but for some, change of work is necessary if they are to have any prospect of continuing in employment. In most of these cases the dominant factor in relation to work is limitation of movement, interfering either with work itself or with the possibility of getting to and from it. Sometimes the disability is more or less confined to the exercise of one particular movement which forms an integral part of the normal working process, and these cases offer a great deal of scope for ingenuity in placing the disabled person in work compatible with his disability, yet sufficiently akin to his previous employment

object, or getting the finger smashed in a slamming door or a closing drawer may result in an enlarged finger joint. The injury is always painful and severe enough to be distinctly remembered. The finger swells promptly, it is sore for several days to weeks, and the bone becomes obviously enlarged.



Hands of a sixty-four year old woman whose fingers began to enlarge at the age of forty-two years. The proximal interphalangeal joints of the left index and middle and the right ring fingers are the site of osteoarthritis as well as most of the terminal joints.

In the course of a few months the finger reaches a stationary condition and no further change takes place. Of course only the injured one or two adjacent fingers are involved. The condition remains unchanged throughout life. (Stecher, 1940). Such enlargements are called *traumatic Heberden's nodes*.

The most interesting and most important form of enlargement of the fingers is the *idiopathic Heberden's node*. These arise spontaneously, starting usually in one forefinger and spreading gradually over a period of several years to many or all fingers on both hands. The disease may begin as "little hard knobs about the size of a pea". These knobs at first may be fluctuant and filled with a gelatinous material, a form which has been described in detail by Gross (1937) and which he called synovial cysts. Such fluctuant cysts are transformed in a few months to bony nodules. The nodular enlargement varies in size from finger to finger and is variously associated progressively with diffuse enlargement and deformity, consisting of flexion and of deviation from the lateral line of the terminal joints. Contrary to general belief, osteoarthritis often involves the proximal finger joints also.

HEBERDEN'S NODES

THE IMPORTANCE OF OSTEOARTHRITIS OF THE FINGERS TO THE PRACTISING PHYSICIAN

By ROBERT M. STECHER, M.D., F.A.C.P.

*From the Department of Medicine of Western Reserve University Medical School,
City Hospital, Cleveland, Ohio.*

HEBERDEN'S nodes are enlargements of terminal joints of the fingers due to osteoarthritis. They occur in several different forms, neither of which is of great significance as a threat to the usefulness of the hands or as forerunners of disability in other parts of the body. Patients are often concerned about their development and frequently consult a physician for advice as to their prevention, their care or their significance. The facts concerning this disease are simple. They are well worth mastering for the confidence and gratitude which the physician enjoys from explaining them to the troubled patient.

The classic description which has so effectively popularized Heberden's name in medical literature is so short and so little known as to be worthy of quotation *in toto* (Heberden, 1803):

"What are those little hard knobs, about the size of a pea, which are frequently seen upon the fingers, particularly a little below the top, near the joint? They have no connexion with the gout, being found in persons who never had it; they continue for life; and being hardly ever attended with pain or disposed to become sore, are rather unsightly than inconvenient, though they must be some little hindrance to the free use of the fingers".

Since Heberden's time, enlargements of the fingers have been variously called "pathognomonic of", "diagnostic of", "typical examples of", "the commonest manifestation of", and "the most benign form of", osteoarthritis. Heberden's original description included only one stage of the disease, which often presents a different appearance, varying widely from the above picture. There may be pea-sized knobs. There may also be enlargements and bony overgrowth with flexion and deviation deformity of the terminal phalanges. Heberden's nodes are confined to the terminal joint but are often associated with osteoarthritis of the proximal interphalangeal joints of the fingers. When this occurs, an erroneous diagnosis of mixed arthritis is sometimes made because of the generally accepted fallacy that arthritis of the proximal joints is always due to rheumatoid arthritis.

PATHOGENESIS

Enlargements of the finger joints arise in two different ways. The most simple and most obvious manner is as a result of direct injury. This is common in young men, and in America is most often due to a direct blow on the end of a finger with a baseball. Any injury to the end of the finger, however, such as a blow with a hammer, the squashing effect of a falling

anterior poliomyelitis or peripheral nerve injury resulting in paralysis, have been observed to prevent the development of Heberden's nodes in the paralysed hand. A stroke, occurring after Heberden's nodes had been well developed, resulted in no important change.

Detailed description of the clinical and *radiological appearances*, with notes on the rate of development of the lesions, have been given elsewhere (Stecher and Hauser, 1948). There was no constant correlation between the clinical appearance and the degree of change revealed by radiology. The most marked radiological change in the shape of spur formation was revealed in lateral views, often when postero-anterior skiagrams seemed nearly normal.

TREATMENT

The treatment of Heberden's nodes is notoriously unsatisfactory. Despite their appearance they are almost symptomless. During their development the fingers are slightly sensitive to mild injury or conventional use. This lasts a few months only in each finger. If aspirin is prescribed for relief the patient often states that the discomfort is not sufficient to warrant that much trouble. An occasional patient will use paraffin packs or other forms of local heat for relief of tenderness. Because of increased sensitiveness to cold, the hands should be protected in the winter time.

In spite of the fact that patients have to be told that the cause of Heberden's nodes is unknown, that nothing can be done to make the finger enlargement go away or to prevent the process from spreading to additional fingers, and that their daughters have a one to two chance of developing similar deformities about the age of fifty, they seem grateful to hear that their disease is not a crippling one, that it will not extend beyond the fingers, and that although they have arthritis, they have the mildest, least disabling and most painless form of the disease. The practitioner can do the patient a great service by protecting her against the futile use of serums, vaccines, or vitamins, which are completely ineffective. Patients accept this advice once they are convinced that they have a self-limited benign disease which cannot lead to disability or invalidism.

References

- Gross, R. E. (1937): *Surg. Gynec. Obstet.*, **65**, 289.
- Heberden, W. (1803): "Commentaries on the History and Cure of Diseases," 2nd edition, London.
- Stecher, R. M. (1940): *New Engl. J. Med.*, **222**, 300.
- (1941): *Amer. J. med. Sci.*, **301**, 801.
- (1944): *J. clin. Invest.*, **23**, 699.
- (1946): *Arch. phys. Med.*, **27**, 409.
- (1946): *J. Lab. clin. Med.*, **31**, 387.
- , and Beard, E. E. (1948): (Unpublished data).
- , and Hauser, H. (1948): *Amer. J. Roentgen*, **59**, 326
- , and Karnosh, L. J. (1947): *Amer. J. med. Sci.*, **213**, 181.

Heredity.—Although the direct cause of idiopathic Heberden's nodes has not been identified, several contributory factors have been described. An extended survey of nearly 7000 individuals revealed that idiopathic Heberden's nodes were much more common, ten to twenty times, in women than in men. Their occurrence was definitely related to age, being rare or unknown in the first three decades of life, with increasing incidence up to about one in three in the ninth decade. The median age was 49.2 years. They had a definite hereditary pattern (Stecher, 1941). The mothers of affected women had Heberden's nodes twice as frequently, and the sisters three times as frequently, as women in the general population. Three actual combinations of familial involvement could not have been expected to occur on a basis of chance alone more often than once in 190, once in 4,500,000, and once in 10,000,000 families. The phenomena observed were best explained by assuming that inheritance was due to a single autosomal factor, sex influenced, so as to be dominant in women and recessive in men. Penetrance depended upon age, not becoming complete until the eighth and ninth decade (Stecher, 1944).

Popular opinion strongly associates Heberden's nodes with *the menopause*. In detailed observations on 99 women it was found that in half of the cases the onset of Heberden's nodes was observed within three years of the last menstrual period. The difference in time between these two events in the other half of the cases varied tremendously. Heberden's nodes preceded the menopause by as much as twenty years and followed the menopause as late as fifteen years. No convincing evidence has yet been presented which explains the manner in which the menopause influences the development of Heberden's nodes (Stecher and Beard, 1948).

Charwomen often say that the deformity of their fingers is due to the hard work they have done or because of the fact that they have had their hands in water so much. These opinions, however, are not convincing, because well-developed Heberden's nodes are often seen on the fingers of women who have never worked.

CLINICAL SIGNS AND SYMPTOMS

Heberden's nodes are a particular manifestation of osteoarthritis confined very largely to the finger joints. Patients with Heberden's nodes seemed to have a higher incidence of creaking knees and to take aspirin for joint stiffness and pain more frequently than did a control group. The association of other joint involvement with Heberden's nodes was not at all alarming (Stecher, 1946). Despite a supposed association of obesity and hypertension with osteoarthritis, no such association in regard to Heberden's nodes was noted (Stecher, 1946). The only condition local to the fingers found to be necessary for the development of Heberden's nodes was an intact nerve supply (Stecher and Karnosh, 1947). Upper motor neurone lesions, such as a hemiplegia and lower motor neurone lesions, as from

the fall of cells in a 100 mm. column of oxalated blood is observed for 1 hour. The blood can be collected by a dry sterilized syringe, by a needle and rubber tube, or in a vacuum ampoule. There is no possibility of an error in dilution upsetting the result, as may happen when measuring citrate and blood mixture in one syringe in the Westergren method, and the Wintrobe tube can later be centrifuged to obtain a hæmatocrit reading. The principles of the test are poorly understood and too much attention should not be given to obtaining precision in the readings. It is as well to set the upper normal limit rather high. I use the following arbitrary system of grading the results into four degrees of abnormal sedimentation and, in following the progress of a case, more attention should be paid to alterations through the grades than to minor numerical fluctuations:—

mm. in 1 hour

	Normal	+	++	+++	++++
Wintrobe	0-9	10-19	20-29	30-39	40 or more
Westergren	0-15	16-30	31-50	51-75	76 or more

Note that the fall in the 200 mm. column of the Westergren tube is not double that in the 100 mm. column of the Wintrobe tube. The above grading is the result of plotting the frequency distribution of large numbers of tests by each method.

When using the test routinely in general medical or surgical cases it is sometimes important to correct the sedimentation rate for anæmia, but severe anæmia, which may greatly mislead in interpreting the result, is not very common in rheumatism and, as a rule, this refinement may be omitted.

Hæmatocrit.—A hæmatocrit reading of the packed red cell volume (P.C.V.) can only be obtained after centrifuging. The cells will not pack to constant volume by gravity alone. A power-driven centrifuge is therefore required to spin the Wintrobe tubes at 3000 r.p.m. for 15 minutes. A small angle centrifuge will do very well and the height of the column of red cells is measured to the mid-point of the sloping surface. The normal range of P.C.V. is 42 to 47 per cent., with an average for both sexes of 44.2 per cent., as obtained by me from 300 subjects with normal blood sedimentation rates and no anæmia. Routine hæmatology is much facilitated by the use of the Wintrobe tube. The technique is as follows:—

Withdraw 5 c.cm. of blood from a vein with a dry needle and mix with 10 mgm. of oxalate mixture (ammonium oxalate 6 mgm., potassium oxalate 4 mgm.). Fill the 100 mm. tube and set up vertically. Read the B.S.R. at the end of 1 hour. Spin the tube in the centrifuge. Read the percentage volume of packed red cells. If the B.S.R. and P.C.V. are normal, no further hæmatological examination need be done in the absence of clinical indications. Estimate the hæmoglobin and red cell count if the P.C.V. is 37 per cent. or below. This will pick out virtually all persons with an anæmia of 85 per cent. hæmoglobin or less. A white cell count may be of value in patients with a raised B.S.R. The count cannot be judged by measurement of the leucocyte cream in the centrifuged tube, as platelets are intermingled with white cells. Only leukæmias with very high counts show up in the hæmatocrit. Icterus of the overlying plasma may also be noted.

Blood picture.—If the hæmatocrit technique is not available, ordinary hæmoglobin, cell count and film methods should be used. Moderate anæmia is almost the rule in rheumatoid arthritis of any duration, especially in females. It is of hypochromic type tending towards microcytic, and the hæmoglobin is reduced more than the red cell count. Some patients with

LABORATORY AIDS IN THE DIAGNOSIS OF RHEUMATISM

By DOUGLAS H. COLLINS, O.B.E., M.D.

Reader in Clinical Pathology, University of Leeds.

NOT so long ago it was hoped that the clinical laboratory could supply all the answers to all the problems of rheumatism. Many biochemical abnormalities were discovered in chronic rheumatism, and practitioners were persuaded to submit their patients for glucose tolerance tests, fractional test meals and so forth but, in fact, the results were of negligible diagnostic value. It then became fashionable to investigate the bacterial flora of most of the body orifices and of the excrements, and vast empires of bacterial colonies were grown in many laboratories and identified with varying degrees of precision. Vaccines were prepared and, for a time, many clinicians found them useful. But it gradually evolved that indiscriminate bacteriological sampling was unhelpful and misleading.

To-day many people consider the sedimentation test to be the only profitable laboratory aid in the diagnosis of rheumatism. Whilst in no way underrating the value of the blood sedimentation rate, which indeed should be estimated in the case of every rheumatic patient, I feel that opinion has taken a too reactionary turn and that the laboratory can render real help in other directions which practitioners often overlook. Anticipating the greater accessibility of clinical laboratory services which is promised, I shall indicate methods which can only be carried out in a fully equipped laboratory, as well as those tests which can be made with little trouble in the consulting room.

HÆMATOLOGY

Sedimentation test.—Everyone now knows how to estimate the blood sedimentation rate and how to interpret the result. It is the most useful test, provided it is remembered that an accelerated rate is of positive value but that a normal rate may occasionally be found with active disease. Patients with rheumatoid disease, ankylosing spondylitis and specific infective arthritis have, with few exceptions, an increased sedimentation rate, whereas patients with osteoarthritis and muscular rheumatism have normal rates unless there is some other concurrent disease. In rheumatic fever and rheumatic carditis a raised sedimentation rate indicates present or very recent activity of the disease. The test is usefully applied in the control of an acute primary attack or relapse since it returns to normal more slowly than the temperature, and when serial readings are made the return of the rate to normal may be taken as indicating the end of the active phase of that particular episode.

I use both the Westergren and Wintrobe techniques but prefer the latter, in which

the fall of cells in a 100 mm. column of oxalated blood is observed for 1 hour. The blood can be collected by a dry sterilized syringe, by a needle and rubber tube, or in a vacuum ampoule. There is no possibility of an error in dilution upsetting the result, as may happen when measuring citrate and blood mixture in one syringe in the Westergren method, and the Wintrobe tube can later be centrifuged to obtain a hæmatocrit reading. The principles of the test are poorly understood and too much attention should not be given to obtaining precision in the readings. It is as well to set the upper normal limit rather high. I use the following arbitrary system of grading the results into four degrees of abnormal sedimentation and, in following the progress of a case, more attention should be paid to alterations through the grades than to minor numerical fluctuations:—

mm. in 1 hour

	Normal	+	++	+++	++++
Wintrobe	0-9	10-19	20-29	30-39	40 or more
Westergren	0-15	16-30	31-50	51-75	76 or more

Note that the fall in the 200 mm. column of the Westergren tube is not double that in the 100 mm. column of the Wintrobe tube. The above grading is the result of plotting the frequency distribution of large numbers of tests by each method.

When using the test routinely in general medical or surgical cases it is sometimes important to correct the sedimentation rate for anæmia, but severe anæmia, which may greatly mislead in interpreting the result, is not very common in rheumatism and, as a rule, this refinement may be omitted.

Hæmatocrit.—A hæmatocrit reading of the packed red cell volume (P.C.V.) can only be obtained after centrifuging. The cells will not pack to constant volume by gravity alone. A power-driven centrifuge is therefore required to spin the Wintrobe tubes at 3000 r.p.m. for 15 minutes. A small angle centrifuge will do very well and the height of the column of red cells is measured to the mid-point of the sloping surface. The normal range of P.C.V. is 42 to 47 per cent., with an average for both sexes of 44.2 per cent., as obtained by me from 300 subjects with normal blood sedimentation rates and no anæmia. Routine hæmatology is much facilitated by the use of the Wintrobe tube. The technique is as follows:—

Withdraw 5 c.cm. of blood from a vein with a dry needle and mix with 10 mgm. of oxalate mixture (ammonium oxalate 6 mgm., potassium oxalate 4 mgm.). Fill the 100 mm. tube and set up vertically. Read the B.S.R. at the end of 1 hour. Spin the tube in the centrifuge. Read the percentage volume of packed red cells. If the B.S.R. and P.C.V. are normal, no further hæmatological examination need be done in the absence of clinical indications. Estimate the hæmoglobin and red cell count if the P.C.V. is 37 per cent. or below. This will pick out virtually all persons with an anæmia of 85 per cent. hæmoglobin or less. A white cell count may be of value in patients with a raised B.S.R. The count cannot be judged by measurement of the leucocyte cream in the centrifuged tube, as platelets are intermingled with white cells. Only leukæmias with very high counts show up in the hæmatocrit. Icterus of the overlying plasma may also be noted.

Blood picture.—If the hæmatocrit technique is not available, ordinary hæmoglobin, cell count and film methods should be used. Moderate anæmia is almost the rule in rheumatoid arthritis of any duration, especially in females. It is of hypochromic type tending towards microcytic, and the hæmoglobin is reduced more than the red cell count. Some patients with

neurological manifestations of pernicious anæmia masquerading as rheumatism appear from time to time in every rheumatism clinic. Absolute leucocytosis is exceptional in chronic arthritis and rheumatism, but in rheumatoid arthritis the polymorphs may show a shift to the left in nuclear pattern (Arneth count).

BLOOD CHEMISTRY

Blood uric acid.—In the absence of leukæmia, blood diseases associated with marked erythroblastosis and azotæmic nephritis, a raised blood uric acid indicates gout. Opinion differs as to whether a patient with gout ever displays a normal blood uric acid. Bauer and Klemperer (1947) state that no patient who has had his first acute attack of gout ever again shows a normal blood urate level, but it is the experience of many that the blood urates fall to normal between the attacks in the early phase of gout with completely symptomless remissions. New technical methods, such as that of Brown (1945), give a high recovery of uric acid from blood filtrates, and serum or plasma gives a more reliable estimation than whole blood (Jacobson, 1938), but whereas the upper normal level of uric acid is about 3.5 mgm. per 100 c.cm. in whole blood, the critical level is 6 mgm. per 100 c.cm. in plasma and serum. Talbott (1943) found the fasting serum uric acid to be over 6 mgm. per cent. in 97 per cent. of gouty patients, and under 6 mgm. per cent. in 98 per cent. of non-gouty subjects.

Blood calcium and phosphorus.—The estimation of these constituents is useful when radiological rarefaction of bone raises the question of hyperparathyroidism. Their values are normal in disuse atrophy of bone and juxta-articular atrophy in arthritis, in senile osteoporosis, and in ankylosing spondylitis, although occasionally there may be a transient increase of blood calcium without diminution of phosphorus in the two latter conditions during the early period of rapidly progressive decalcification.

Blood phosphatase.—*Serum alkaline phosphatase* increase is a measure of osteoblastic activity. It is found in many bone diseases and tumours and is especially high in Paget's disease. It is normal in disuse atrophy and senile osteoporosis in which bone regeneration is at a standstill. *Serum acid phosphatase* usually refers to the prostatic acid phosphatase and is increased in metastasizing prostatic carcinoma. It is not increased in osseous carcinomatosis originating from breast or lung which are the most common primary sites of cancer spreading to bone.

URINE ANALYSIS

Never omit to examine the urine of a patient complaining of rheumatic symptoms, including microscopy of the centrifuge deposit. I have several times met with diabetic patients whose neuritic pains have passed under the label of fibrositis for a dangerously long time through the physician neglecting to test the urine for sugar. A patient with chronic gout may complain of passing gravel. It is important to identify as urates any small

insoluble particles and this may be done by the murexide test which is described on page 184 in connexion with tophi. Except for research purposes in investigating the cycle of the acute gout attack the estimation of the total output of uric acid derivatives is of no value. The presence of casts and red blood cells in the urine deposit is related to general medical conditions, but the finding of pus may have a direct bearing on rheumatic complaints. In both sexes and at all ages chronic lumbar pain can be the presenting symptom of a low-grade pyelitis. Any urinary tract infection can aggravate, although it may never cause, an arthritis. I have known the discovery of a few pus cells in the urine lead to the diagnosis of gonorrhœa when there was no manifest urethral discharge or gleet. If such a diagnosis can be established by this means in an arthritic case, prostatic massage and manipulations which carry the risk of disseminating the infection can thereby be avoided. The examination is made thus:—

Obtain a morning urine specimen, centrifuge and examine the deposit under the microscope. If there are even only a few pus cells, make a film by pulling the coverslip off the end of the slide or by picking up some more of the deposit and smearing it out between two slides. Allow to dry and stain by Gram's method, preferably counterstaining with a mixture of neutral red (0.25 per cent.) and weak carbol fuchsin. In this way pus cells are well preserved and delicately stained so that intracellular diplococci can be readily recognized. Confirmation by culture may be difficult.

BACTERIOLOGICAL METHODS

The indiscriminate swabbing of, and preparation of cultures from, nose, throat, teeth or stools in every case of rheumatism is now known to be futile. Treat any obviously active focus of infection in the hope, but not in the expectation, of ameliorating the rheumatic condition. Take cultures therefrom as a matter of interest but not with a view to obtaining a precise diagnosis or giving specific treatment. Search for the hidden focus with the eye, the finger and the X-ray but not with the swab and the platinum loop.

Blood cultures are sterile in rheumatic fever and rheumatoid arthritis. They are called for in every case of prolonged pyrexia of uncertain origin. Subacute bacterial endocarditis, chronic meningococcal septicæmia and brucellosis sometimes cause severe arthralgia or manifest polyarthritis.

Agglutination tests are available for the diagnosis of enteric fevers, dysentery, brucellosis (undulant fever), and Weil's disease, which may cause arthritis or muscle and joint pain. In Weil's disease animal inoculation with urine deposit is a more reliable procedure. In 60 to 80 per cent. of patients with rheumatoid arthritis the serum agglutinates group A hæmolytic streptococci (Kalbak, 1947). The test is negative in rheumatic fever and in health. Unfortunately the technique is difficult, as standardized streptococcal antigens are not available and few laboratories will be prepared to undertake it as a routine test.

The Wasserman and Kahn tests may be indicated on various grounds, but syphilitic arthritis is exceedingly rare. Syphilis affects the joints (1)

in infants as an epiphysitis; (2) in late congenital lues as symmetrical painless hydrarthrosis (Clutton's joints); (3) in adults very occasionally as gummatous osteitis eroding the articular ends of bones or as periostitis. The most common joint lesion in syphilis is Charcot's joint. This occurs in a small proportion of tabetics in whom serological tests are sometimes negative. It is a neuropathic and not a syphilitic condition, as an identical lesion is met with in syringomyelia.

The gonococcal complement fixation test may provide a clue to the gonorrhœal origin of an arthritis when smears and cultures are negative. The behaviour of the test in the course of a gonococcal infection is, however, somewhat unpredictable. If a gonococcal focus remains, so may the complement fixing antibodies persist for many years, but often, in a case of arthritis which but for the history is indistinguishable from rheumatoid arthritis, the test is so weak or negative that there is no means of deciding whether gonococcal infection caused the arthritis or merely provoked the onset or relapse of a non-specific rheumatoid condition. Suppurative gonococcal arthritis is rare nowadays. The venereologist probably sees most cases of true gonorrhœal rheumatism, which takes the form of a transient arthralgia or synovitis with effusion appearing about two to six weeks after the acute urethritis.

ASPIRATION OF SYNOVIAL EFFUSION

With proper aseptic precautions this little operation may be safely done on any of the larger joints when the distended synovial sac lies not too deeply below the skin. It is demanded when suppuration within a joint is suspected, and if pus is withdrawn it must be sent for examination in a sterile container for the bacteriologist to identify the organism and to test its sensitivity to penicillin. The fluid in rheumatoid arthritis and in rheumatic fever is moderately turbid, with a cell count of about 20,000 leucocytes per c.mm., of which about 70 per cent. are polymorphs. Cultures are sterile. The fluid in osteoarthritis and in chronic traumatic synovitis due to internal derangement of the joint is quite different, showing only a few hundred leucocytes per c.mm. with no more than 10 or 20 per cent. of polymorphs. A traumatic effusion always shows blood, altered blood or icterus with a positive van den Bergh reaction. Diagnostic aspiration is of real value when the cause of a chronic effusion is in doubt.

BIOPSY METHODS

Tophi.—Difficulty may arise in deciding whether or not a structure that looks like a tophus is really a tophus, and the diagnosis of gout may depend upon identifying urates therein. The murexide test is simple to use.

Squeeze or pick out a fragment of the chalky centre of the nodule. Mix it into a paste with two or three drops of concentrated nitric acid on a porcelain surface using a glass rod. Add a few drops of weak ammonia (about 5 c.cm. of concentrated

ammonia in half a test tube of water). A red colour turning to a deep red purple indicates the presence of urates.

Subcutaneous nodules in rheumatoid arthritis.—These have a distinctive histological structure (Collins, 1937) and biopsy and section of a nodule sometimes provide confirmatory evidence in the diagnosis of rheumatoid arthritis. No such formations occur in osteoarthritis. The nodules of rheumatic fever are smaller and can usually be distinguished when sectioned. When there are one or two small nodes around the finger joints and some uncertainty about the presence of actual joint disease, a biopsy is well worth while. I have several times found some non-arthritic condition in such circumstances, the nodule proving on section to be a giant-cell tendon sheath tumour, a neurofibroma, a xanthoma, or some other lesion.

Muscle biopsy has been recommended as a diagnostic method, as focal cellular infiltrations occur in the muscles in rheumatoid arthritis. But the procedure is not as simple as cutaneous biopsy and focal myositis is not a specific lesion of rheumatoid disease, having been found in many other conditions (Clawson, Noble and Lufkin, 1947).

Various *skin diseases* may masquerade as rheumatism or occur in rheumatism, and biopsy will assist the diagnosis, e.g. erythema nodosum, lupus erythematosus, xanthoma tuberosum, scleroderma, dermatomyositis, neurofibromatosis, and polyarteritis nodosa.

Fibrositic nodules cannot be defined pathologically. Either they are so deeply situated that attempts at their removal fail, or no structural tissue changes exist in this condition. The only "fibrositic" nodules I have received for examination have been ill-defined lumps of normal fat or fibrofatty tissue, or nodular lesions of one of the conditions mentioned in the preceding paragraph.

Regional lymph glands.—Biopsy of an inguinal lymph gland may reveal tubercles early in the course of tuberculous arthritis of the knee or ankle (Seddon, 1939). Glands elsewhere draining other joints have also been examined when appropriate. Although this line of investigation is not infallible and may occasionally yield both false negative and false positive answers, it may often give strong support to a diagnosis of tuberculosis before any X-ray changes are visible (Arden and Scott, 1947). The lymph glands in rheumatoid arthritis and Still's disease show only non-specific inflammatory changes.

References

- Arden, G. P., and Scott, J. C. (1947): *Brit. med. J.*, ii, 87.
 Bauer, W., and Klemperer, F. (1947): in "Diseases of Metabolism," edited by G. G. Duncan, 2nd edition, Philadelphia and London, p. 611.
 Brown, H. (1945): *J. biol. Chem.*, 158, 601.
 Clawson, B. J., Noble, J. F., and Lufkin, N. H. (1947): *Arch. Path.*, 43, 579.
 Collins, D. H. (1937): *J. Path. Bact.*, 45, 97.
 Jacobson, B. M. (1938): *Ann. intern. Med.*, 11, 1277.
 Kalbak, K. (1947): *Ann. rheum. Dis.*, 6, 230.
 Seddon, H. J. (1939): *Brit. med. J.*, i, 105.
 Talbott, J. H. (1943): "Gout," edited by H. A. Christian, New York.

A CRITICAL SURVEY OF THE PRESENT POSITION IN THE TREATMENT OF THE MORE COMMON SPECIFIC FEVERS

By J. L. FLUKER, M.B., M.R.C.P., D.P.H.

Deputy Medical Superintendent, City Isolation Hospital, Plymouth.

THROUGHOUT history, mankind has been scourged with lethal pestilences which have decimated not only cities but even whole continents. The plague of Athens in 430 B.C., so trenchantly described by Thucydides, and the Black Death of 1348 A.D., are but single examples of each. In comparatively recent years, smallpox, cholera, typhoid fever, typhus and many other fell diseases were accepted as a matter of course and extensive outbreaks evoked little comment. Preventive medicine, through such measures as vaccination, preventive inoculation and improved sanitation in the widest sense, has almost banished these pestilences, but other diseases still remain with us, exerting direr effects than is often realized, not only from a not insubstantial mortality, but also from crippling and permanent sequela. Preventive and curative medicine are the two main weapons of counter-attack, and this year marks the centenary of the first great Public Health Act of 1848 which, with all its shortcomings, was a landmark in the history of the former. The latter, with which this article is concerned, has been revolutionized by the respective discoveries of the sulphonamides by Domagk in 1933, and of penicillin by Fleming in 1929, with their subsequent widespread applications to clinical medicine.

This article, so far as possible, is based on personal experience, but where this is lacking, and in many other instances, the much more important work of others is referred to in an attempt to evaluate the soundest methods of treatment from the viewpoint of the ordinary practitioner. Not all infective diseases are included, some, for example puerperal pyrexia, are excluded from lack of recent experience and others, e.g. venereal diseases, a separate subject in themselves, in the interests of space. Staphylococcal infections have also been excluded.

THE PNEUMONIAS

Lobar pneumonia.—In pre-sulphonamide days, the total mortality for lobar pneumonia exceeded 20 per cent., although it was much lower in the age-groups from five to forty. Sulphonamides reduced the figure to about 10 per cent., but the response in the elderly was less satisfactory. The case for the use of the sulphonamides was unanswerable but the question now is to what extent they should be supplemented with, or superseded by, penicillin.

In vitro, Ungar (1943) showed that the simultaneous addition of a sulphonamide to penicillin would give the same result against the pneumococcus as twice the

amount of the latter alone. Collen *et al.* (1946) tried the use of penicillin and sulphadiazine both combined and separately in 1,620 cases and stated: "... the adjuvant use of penicillin . . . in severely ill patients resulted in a decrease of mortality rate from 26.9 to 6.7 per cent. The over-all mortality rate was decreased from 6.2 to 1.5 per cent." Sulphonamide-treated cases without penicillin had a mortality of 1.5 per cent. Anderson and Ferguson (1945), in a double series of 63 cases treated respectively with sulphonamides and penicillin, had the impression that three cases were definitely saved by the latter. Kinsman *et al.* (1945) treated 100 cases with sulphadiazine and 75 cases with penicillin, obtaining equal results in both series.

Personal experience would indicate that in the average case there is little to choose but that on occasion penicillin is life-saving; for example, a naval sick-berth artificer, aged nineteen, who, overwhelmed with toxæmia, not only failed to respond but showed intolerance to sulphonamides and only painfully improved after twenty-four hours following the substitution of penicillin therapy. Sulphonamides, easier to administer, are the treatment of choice in the average patient of under forty years of age. Penicillin alone is indicated in instances of sulphonamide intolerance, drug-fast organisms and failure to respond within thirty-six hours, increased toxæmia within twenty-four hours, and in most patients over forty, and almost all over sixty; also in patients with an initial low polymorphonuclear count, renal disease, threatened cardiac failure, alcoholism and obesity. Indications for combined therapy (not to be applied indiscriminately), in addition to combinations of two or more of the above factors, include severe toxæmia or circulatory failure, rapid deterioration, severe cases late in beginning treatment, and apparently those with high pneumococcal sputum counts or type III infections (Collen *et al.*, 1946). The clinical condition, however, should always be the main guide.

Occasionally a patient may fail to respond to penicillin and yet subsequently react to sulphonamides:—

A man of fifty-five, with a right lower lobe pneumonia, moderate toxæmia and considerable dyspnoea in part due to a concomitant emphysema, failed to respond to penicillin and, despite 360,000 units intramuscularly, after about forty hours his condition had deteriorated. Sulphadiazine was substituted with a rapid response, and at the end of a further three days he was much better and apyrexial.

Scadding (1946) has shown that a course of only 100,000 to 150,000 units of penicillin may lead to a subsequent satisfactory therapeutic response to sulphonamides; an observation which might apply to the above case.

It has sometimes been said that the sulphonamide treatment of *broncho-pneumonia* is unsatisfactory. In elderly people this may in part be true. In infants, however, it is not so, and with good nursing the mortality has been reduced in most hospitals to very low proportions. The arguments outlined above apply here in the main with three additional indications for penicillin in babies, namely, all those aged less than two years when the condition is a complication of pertussis, prematurity, and in the presence of marked dehydration. Two illustrative cases (Fluker, 1946a) will show the beneficial effects of penicillin:—

(a) A girl aged eighteen months was admitted to hospital with a five-day history of spasmodic cough, vomiting and increasing dyspnoea. She had received an in-

adequate dosage of sulphathiazole for the previous four days, $\frac{1}{2}$ gm. four-hourly. She was very ill with pertussis and broncho-pneumonia and markedly cyanosed. Sulphadiazine in full doses, $\frac{1}{2}$ gm. four-hourly, was started, but after twenty-four hours she was much worse. The drug was withdrawn and penicillin in oil, 100,000 units intramuscularly twice a day, substituted to a total of 800,000 units, with an additional 85,000 units of aqueous penicillin in five divided doses. She made a rapid recovery although a tiresome cough persisted for a further month.

(b) A baby of six weeks was admitted cyanosed and moribund, temperature 99.2° F. (37.3° C.), pulse rate 128 per minute, respiratory rate 48 per minute, with broncho-pneumonia and the history of a week's illness. Two days before admission she had developed a squint and in the preceding twelve hours had had repeated convulsions. Sulphathiazole, $\frac{1}{2}$ gm. four-hourly, had been given for six days, so penicillin was given instead, six injections of aqueous solution intramuscularly, totalling 90,000 units, and eight of penicillin in oil, totalling 800,000 units. To the surprise of all, she steadily, if slowly, improved and was discharged some ten weeks later, fit and well, although after a protracted convalescence.

The usual dose of penicillin ranges from 600,000 to 1,600,000 units for pneumonia. Although, theoretically, it is best given at three-hourly intervals, the results seem equally satisfactory if it is given in three, or even two, daily doses of 100,000 units in aqueous solution. Despite its use in the above cases, penicillin in oil would appear to be less satisfactory than in aqueous solution. If in doubt, penicillin should be given in preference to sulphonamides.

STREPTOCOCCAL INFECTIONS

Tonsillitis.—In both tonsillitis and scarlet fever, a number of observers, e.g. Plummer *et al.* (1945), have found penicillin superior to sulphadiazine in ridding the throat of organisms.

They used 15,000 units four-hourly and found it necessary to continue treatment for six days in tonsillitis, in order to prevent both bacteriological and clinical relapse. Jersild (1948) confirms these results. Even so, in one case of Plummer's there was a severe relapse. Long (1946) believes that a dosage of not less than 500,000 units daily "... is sufficient to remove all penicillin-sensitive organisms from the mouth. In addition the same dosage seems to act dramatically in the few cases ... of the very severe anginose scarlet fever so treated. The effect is rapid and treatment need only be continued for three days". Macgregor and Long (1944), and Robinson (1945), claim satisfactory results from the use of penicillin pastilles sucked in the mouth in streptococcal throat infections, although the latter states that the results are less satisfactory than with systemic penicillin.

Because so many normal subjects are carriers, throat swabs positive for hæmolytic streptococci are not of great value in most cases of tonsillitis or scarlet fever, nor in the latter disease, in contrast to diphtheria, are release cultures a reliable guide as to whether or not a case has ceased to be infective. Again, it is not known how many people apparently freed from the organism by treatment have subsequently relapsed bacteriologically, say six months later. Therefore, in tonsillitis, it is necessary to rely mainly upon clinical indications for chemotherapy. These are: œdema or swelling, marked pain, redness and extensive exudate, in that order of importance. The slightest suggestion of œdema should indicate treatment, as often a peritonsillar abscess may be avoided before pus has had a chance to form. Penicillin is the drug of choice, and dosage should be on the lines indicated

above and continued in all cases for at least forty-eight hours after symptoms have disappeared so as to diminish the likelihood of a relapse. Conversely, most cases of simple pharyngitis and even of mild follicular tonsillitis do not seem to benefit from chemotherapy and a number of cases are treated unnecessarily.

Scarlet fever.—It is now generally accepted that sulphonamides have little or no effect either upon the course of scarlet fever or in the prevention of complications (Candell and Burwell, 1946), and their use at Plymouth has long since been discontinued except in certain complications, such as early or late cervical adenitis, or in otitis media, when they are of undoubted value. In both of these conditions, however, penicillin would appear to be of greater efficacy. In the former, in at least four cases ineffectively treated with sulphonamides, the use of penicillin dispensed with what had seemed to be an inevitable recourse to surgery. In an uncomplicated case of the anginose type, penicillin should be used as well as serum, as a few promising results have thus been obtained (Long, 1946). With regard to mild cases, which fortunately are the general rule to-day, the question is not settled. Clinically, penicillin has less effect than serum, which should always be given except in cases of suspected or known hypersensitivity (Meads *et al.*, 1945). For cases treated at home or separately in strict isolation, serum alone might well be adequate.

Weiss and Manheims (1946), however, claim that penicillin is of value in the prevention of otitis media. In the absence of contrary statement it is presumed that their cases were treated in open scarlet fever wards. In that respect, in view of the bacteriological findings already mentioned, the drug might prove of value in prevention of cross infection, and particularly in a reduction of the period of infectivity. A recent article by Jersild (1948) is of importance in this respect, and he has published a series of 3000 cases treated with penicillin, 90,000 to 150,000 units twice daily for six days being the dosage. It is perhaps a pity that a direct comparison was not made between penicillin and the results of serum treatment instead of sulphonamides. Not only was penicillin found to be markedly superior to sulphonamides in otitis media, but in uncomplicated cases the duration of stay in hospital was reduced to eight days.

From what has already been said, this result would be expected on theoretical grounds. Current practice would offer additional support, and one advantage of penicillin treatment seems to be a reduction in the number of cases of post-scarlatinal rhinitis. The present position, then, would seem to be that all cases of scarlet fever in open wards should receive penicillin as an adjuvant to serum, on the lines suggested by Jersild (1948) or Long (1946). Although further work is needed, and the medico-legal aspect still has to be borne in mind, it does seem that penicillin may have an important part to play in the reduction of the period of infectivity and the consequent freeing of hospital beds. The number of return cases will provide the final answer.

Acute nephritis is a notorious complication of tonsillitis and scarlet fever and, in view of its apparent association with the streptococcus, chemotherapy has been advocated. As, however, nephritis is part of a generalized

adequate dosage of sulphathiazole for the previous four days, $\frac{1}{2}$ gm. four-hourly. She was very ill with pertussis and broncho-pneumonia and markedly cyanosed. Sulphadiazine in full doses, $\frac{1}{2}$ gm. four-hourly, was started, but after twenty-four hours she was much worse. The drug was withdrawn and penicillin in oil, 100,000 units intramuscularly twice a day, substituted to a total of 800,000 units, with an additional 85,000 units of aqueous penicillin in five divided doses. She made a rapid recovery although a tiresome cough persisted for a further month.

(b) A baby of six weeks was admitted cyanosed and moribund, temperature 99.2° F. (37.3° C.), pulse rate 128 per minute, respiratory rate 48 per minute, with broncho-pneumonia and the history of a week's illness. Two days before admission she had developed a squint and in the preceding twelve hours had had repeated convulsions. Sulphathiazole, $\frac{1}{2}$ gm. four-hourly, had been given for six days, so penicillin was given instead, six injections of aqueous solution intramuscularly, totalling 90,000 units, and eight of penicillin in oil, totalling 800,000 units. To the surprise of all, she steadily, if slowly, improved and was discharged some ten weeks later, fit and well, although after a protracted convalescence.

The usual dose of penicillin ranges from 600,000 to 1,600,000 units for pneumonia. Although, theoretically, it is best given at three-hourly intervals, the results seem equally satisfactory if it is given in three, or even two, daily doses of 100,000 units in aqueous solution. Despite its use in the above cases, penicillin in oil would appear to be less satisfactory than in aqueous solution. If in doubt, penicillin should be given in preference to sulphonamides.

STREPTOCOCCAL INFECTIONS

Tonsillitis.—In both tonsillitis and scarlet fever, a number of observers, e.g. Plummer *et al.* (1945), have found penicillin superior to sulphadiazine in ridding the throat of organisms.

They used 15,000 units four-hourly and found it necessary to continue treatment for six days in tonsillitis, in order to prevent both bacteriological and clinical relapse. Jersild (1948) confirms these results. Even so, in one case of Plummer's there was a severe relapse. Long (1946) believes that a dosage of not less than 500,000 units daily ". . . is sufficient to remove all penicillin-sensitive organisms from the mouth. In addition the same dosage seems to act dramatically in the few cases . . . of the very severe anginous scarlet fever so treated. The effect is rapid and treatment need only be continued for three days". Macgregor and Long (1944), and Robinson (1945), claim satisfactory results from the use of penicillin pastilles sucked in the mouth in streptococcal throat infections, although the latter states that the results are less satisfactory than with systemic penicillin.

Because so many normal subjects are carriers, throat swabs positive for hæmolytic streptococci are not of great value in most cases of tonsillitis or scarlet fever, nor in the latter disease, in contrast to diphtheria, are release cultures a reliable guide as to whether or not a case has ceased to be infective. Again, it is not known how many people apparently freed from the organism by treatment have subsequently relapsed bacteriologically, say six months later. Therefore, in tonsillitis, it is necessary to rely mainly upon clinical indications for chemotherapy. These are: œdema or swelling, marked pain, redness and extensive exudate, in that order of importance. The slightest suggestion of œdema should indicate treatment, as often a peritonsillar abscess may be avoided before pus has had a chance to form. Penicillin is the drug of choice, and dosage should be on the lines indicated

infection, are indications for chemotherapy—sulphonamides in the first instance and penicillin in the others.

Typhoid fever still recurs from time to time.

Bigger (1946) showed that *in vitro* the combination of penicillin and sulphathiazole . . . kills large numbers of typhoid bacilli. McSweeney (1946) treated six cases with both penicillin and sulphathiazole, four of them receiving two courses each comprising 10,000,000 units . . . and 34 gm. given in four days. There was an interval of two to three days between each course. "Speedy disappearance of toxæmia, subsidence of pyrexia and disappearance of organisms from blood, fæces and urine followed the end of the second course in three of the four cases". In the fourth case, there was a relapse after a fortnight "which rapidly subsided when the second course was initiated". Bevan *et al.* (1948), who treated 39 patients from the Aberystwyth outbreak, did not observe the speedy disappearance of toxæmia and subsidence of pyrexia described by McSweeney, and he considered it necessary to warn against the indiscriminate use of penicillin-sulphathiazole in the treatment of typhoid fever. Of five of their patients treated with Felix's anti-typhoid serum (Vi + O) "four promptly showed definite improvement". Parsons (1948) concluded that ". . . penicillin and sulphonamides would have to produce much more dramatic results in the way of a rapid cure . . . if the disturbance . . . of repeated injections was to be counterbalanced", but added that in his series all of McSweeney's conditions "were not strictly followed". McSweeney (1948), who has successfully treated a further 28 cases, criticizes in particular the Aberystwyth series on the grounds that the majority of cases were "not treated in the way suggested". He also states that serum should be given early in the disease. (That, surely, is a cardinal principle of serotherapy, no matter what the disease.) Dana (1948) states that "we have here therapeutic agents which, although not specific, if used correctly, improve the prospects in severe typhoid fever . . . The mortality of typhoid fever in my service was reduced last year to about 3 per cent."

Clearly the question is still *sub judice* and further carefully controlled work is required on the lines suggested by McSweeney. If possible, the organisms should be subjected beforehand to *in vitro* tests to determine sensitivity and the dosage of penicillin recommended regarded as the minimum. Haphazard treatment of isolated cases cannot be condemned too strongly. In Plymouth no striking success has been obtained with these reagents, although lack of opportunity has prevented a trial on McSweeney's lines.

Undulant fever, inseparable from enteric from the aspect of differential diagnosis, partly responds to sulphonamide treatment. Owing to the often severe accompanying leucopenia, the white count should be watched closely. Failing sulphonamides, "fouadin", an antimony compound, is often of value (Harries and Mitman, 1947). The dose is 1.5 c.cm. on the first day, 3 c.cm. on the second, and thereafter 5 c.cm. (4.5 c.cm. for females) on alternate days. Penicillin is ineffective.

VIRUS DISEASES

In general, there are no effective chemotherapeutic reagents available, with one or two exceptions in the large group of diseases caused by filtrable viruses. Sulphonamides are effective against *lymphogranuloma inguinale* and *trachoma*. Penicillin in large doses is apparently of value in *psittacosis* (Bedson and May, 1945), the *rickettsia of typhus*, although ordinary doses are here ineffective, and *inclusion conjunctivitis* in which Sorsby (1945) has

capillary disorder throughout the body, probably a late sensitization phenomenon to the streptococcus which is never found in the kidney, it is difficult to explain the rationale of this viewpoint. Anyhow, sulphonamides are contraindicated and in an ordinary case penicillin seems to be without benefit. Sen (1946) states that "it is not necessary for normal cases". The *Lancet* (1946) adds that "a controlled assessment is necessary". Sen (1946) also states that "it may be worth trying for very severe cases when there is a complicating infection". This is a very different matter, and if an acute focus of infection, such as tonsillitis or otitis media, is present, it is wise to give penicillin as suggested by Moncrieff (1944) and Shore (1944); it is essential in the presence of erysipelas.

Erysipelas.—For ordinary cases, sulphonamides are the first choice, with penicillin to fall back upon in the event of troublesome relapse or sulphonamide intolerance. Associated with nephritis, and in particular with uræmia, erysipelas, even to-day, is often a terminal event, and in such conditions I have yet to see a satisfactory response to sulphonamide therapy. Such a combination is a major indication for penicillin as is shown in the following case:—

A man of fifty-eight was admitted to hospital with extrarenal uræmia (blood urea over 150 mgm.), and retention of urine with overflow due to an enlarged prostate. He had erysipelas of the thigh and face. After thirty-six hours of sulphadiazine therapy, both the local and general condition had deteriorated. Replacement of sulphadiazine with penicillin led to rapid improvement and in three days, despite continued uræmia, his skin was normal.

The corollary is that the recognition of uræmia, especially if extrarenal, in association with erysipelas, is of paramount importance.

ALIMENTARY INFECTIONS

The next group of diseases for consideration are the more common alimentary infections occurring in this country, notably bacillary dysentery, infantile gastro-enteritis, and enteric (typhoid and paratyphoid) fevers.

In *bacillary dysentery*, sulphaguanidine and succinyl-sulphathiazole are commonly recommended and give satisfactory results, but sulphathiazole and sulphadiazine may also be used. Indeed, Scadding (1945) considers that the latter is the most efficacious. According to Brewer (1944), succinyl-sulphathiazole is the drug of choice in the treatment of carriers, particularly of the Sonne carrier, which is of the most practical importance in this country.

Infantile gastro-enteritis.—In the majority of cases no causal organism can be found, and then chemotherapy is of little avail. It has been suggested that excessive coliform fermentation produces toxins responsible for liver damage, in which event sulphonamides should logically be employed (Gunn, 1945). In practice, their use is disappointing. Henderson (1943) found that sulphaguanidine was of benefit but, apart from its use in frank dysentery, this is not the general opinion. Those cases which complicate measles, for example, or in which there is a concomitant broncho-pneumonia or mastoid

103° F. (39.4° C.), and a marked constitutional disturbance. The Paul Bunnell test was strongly positive. She remained ill for a week and then suddenly recovered.

(b) A W.R.N.S. rating, aged twenty-six, was being investigated in the venereal diseases department. One day after receiving a provocative dose of 0.45 gm. of stabilarsan she developed a typical, severe and prolonged attack of the anginose type of glandular fever.

Ordinary *influenza* is uninfluenced by specific drugs although they are all too frequently given, presumably in the hope of avoiding more serious complications. It is doubtful whether in fact this end is achieved, nor do the tracheitis and bronchiolitis which often occur as part of the disease appear to be influenced. Fortunately the classically acute influenzal pneumonia with heliotrope cyanosis is not often seen nowadays. This condition is a major indication for penicillin.

A female patient, aged forty-five, was seen who had been ill with influenza for the previous twenty-four hours. Two hours before the consultation she had developed heliotrope cyanosis and two hours later, despite the immediate intravenous administration of 100,000 units of penicillin, she was dead.

In such cases, early recognition and expert nursing are of prime importance, and the simultaneous administration of sulphadiazine would seem wise.

Since 1940, all cases of *measles* in the Plymouth Isolation Hospital, whether complicated or not, have received routine sulphonamide treatment, and it was practically unheard of for any straightforward case to develop complications while in hospital. This practice was being followed by Banks, at any rate in 1942, who gave the drug for five days. Since neither penicillin nor sulphonamides have any direct effect upon the uncomplicated disease, it is argued by some that their routine use is unjustifiable. In the case of penicillin that is no doubt true on account of the necessity for injections, but those who do give sulphonamides hold that the resulting freedom from unpleasant complications provides full justification. It might further be objected that this argument is inconsistent with the observations on influenza. Measles, however, is a well-defined condition, whereas "influenza", that diagnostic scrap-heap, is applied to a whole host of completely unrelated conditions which would thus tend to increase the indiscriminate use of sulphonamides; a dangerous practice wholly to be condemned. So far as complicated cases are concerned, for at least eight years the mortality has been *nil*. This includes ten cases of measles and laryngeal diphtheria. Although expert nursing played an indispensable part in this satisfactory result, sulphonamides must claim a substantial share of the credit. Most hospitals now report a mortality of about 0.3 to 0.5 per cent. as opposed originally to about 3 per cent. Penicillin should be given to severe cases on the general lines already indicated, and it must be remembered that there is no effective specific treatment against measles encephalomyelitis.

PERTUSSIS

Pertussis is responsible for a higher mortality rate among young children than any other specific fever, although the public seems scarcely aware of

obtained "dramatic results". The most promising line of treatment with typhus would appear to be para-aminobenzoic acid, and Yeomans *et al.* (1944) state that "... large doses of para-aminobenzoic acid exert a definite beneficial effect on the course of louse-borne typhus if treatment is started in the first week". The initial loading dose was from 4 to 8 gm., followed by 2 gm. two-hourly to an average total of 127 gm.

For the following virus diseases, specific chemotherapy is lacking:—Mumps, rubella, rabies, acute anterior poliomyelitis, infective hepatitis, herpes zoster, herpes simplex, coryza, primary atypical pneumonia (pneumonitis), erythema infectiosum, exanthema subitum, acute lymphocytic choriomeningitis, encephalitis lethargica, acute disseminated encephalomyelitis (often itself complicating another virus infection), equine encephalomyelitis, yellow fever, vaccinia, varicella, variola, glandular fever, influenza and measles. The last five require further discussion.

The very severe and now fortunately rare form of *varicella*—*varicella gangrenosa*—which is the result of secondary infection of the lesions, either with hæmolytic streptococci or the Klebs-Loeffler bacillus, would in all probability benefit greatly from penicillin, although, in the latter instance, serum is essential.

In *variola* neither sulphonamides nor any other known drugs have a specific action on the initial stages (Wilkinson, 1942). Chemotherapy, particularly penicillin, has an important part in the treatment of secondary fever, above all in confluent cases, whereby much scarring may be avoided. No remedy is likely to be effective in *variola hæmorrhagica pustulosa* and still less in *purpura variolosa*, but penicillin should be tried, especially if the patient survives to the later phases. The foregoing is borne out by recent findings in the 1947 Staffordshire outbreak when there were thirty cases with eight deaths. Five cases were hæmorrhagic, all fatal, and "eight were confluent, only one of which was fatal". The latter were treated with penicillin "and this may account for their low mortality" (*Medical Officer*, 1948).

Glandular fever.—Numerous remedies have been advocated, of which only the sulphonamides, penicillin and organic arsenicals merit consideration. Sulphonamides are valueless and, in view of the more than occasional occurrence of a severe polymorphonuclear leucopenia (the absolute count was only 1,200 in a recent case), contraindicated. Penicillin has no effect, although it is not infrequently given even to recovering cases. A threatened peritonsillar abscess, a relatively rare complication, would, of course, be an indication. Organic arsenicals have been advocated, especially by Smith and Shaw (1945), who treated six cases. In this connexion, brief mention of two cases, both of which occurred before the date of their article, may be of interest.

(a) A student nurse, aged nineteen, reported with what appeared to be a typical Vincent's angina. She was given stabilarsan, 0.45 gm. intravenously. On the following day, despite a marked improvement in her throat condition, she developed a generalized lymphadenitis, an erythematous rash all over the trunk, pyrexia of over

103° F. (39.4° C.), and a marked constitutional disturbance. The Paul Bunnell test was strongly positive. She remained ill for a week and then suddenly recovered.

(b) A W.R.N.S. rating, aged twenty-six, was being investigated in the venereal diseases department. One day after receiving a provocative dose of 0.45 gm. of stabilarsan she developed a typical, severe and prolonged attack of the anginose type of glandular fever.

Ordinary *influenza* is uninfluenced by specific drugs although they are all too frequently given, presumably in the hope of avoiding more serious complications. It is doubtful whether in fact this end is achieved, nor do the tracheitis and bronchiolitis which often occur as part of the disease appear to be influenced. Fortunately the classically acute influenzal pneumonia with heliotrope cyanosis is not often seen nowadays. This condition is a major indication for penicillin.

A female patient, aged forty-five, was seen who had been ill with influenza for the previous twenty-four hours. Two hours before the consultation she had developed heliotrope cyanosis and two hours later, despite the immediate intravenous administration of 100,000 units of penicillin, she was dead.

In such cases, early recognition and expert nursing are of prime importance, and the simultaneous administration of sulphadiazine would seem wise.

Since 1940, all cases of *measles* in the Plymouth Isolation Hospital, whether complicated or not, have received routine sulphonamide treatment, and it was practically unheard of for any straightforward case to develop complications while in hospital. This practice was being followed by Banks, at any rate in 1942, who gave the drug for five days. Since neither penicillin nor sulphonamides have any direct effect upon the uncomplicated disease, it is argued by some that their routine use is unjustifiable. In the case of penicillin that is no doubt true on account of the necessity for injections, but those who do give sulphonamides hold that the resulting freedom from unpleasant complications provides full justification. It might further be objected that this argument is inconsistent with the observations on influenza. Measles, however, is a well-defined condition, whereas "influenza", that diagnostic scrap-heap, is applied to a whole host of completely unrelated conditions which would thus tend to increase the indiscriminate use of sulphonamides; a dangerous practice wholly to be condemned. So far as complicated cases are concerned, for at least eight years the mortality has been *nil*. This includes ten cases of measles and laryngeal diphtheria. Although expert nursing played an indispensable part in this satisfactory result, sulphonamides must claim a substantial share of the credit. Most hospitals now report a mortality of about 0.3 to 0.5 per cent. as opposed originally to about 3 per cent. Penicillin should be given to severe cases on the general lines already indicated, and it must be remembered that there is no effective specific treatment against measles encephalomyelitis.

PERTUSSIS

Pertussis is responsible for a higher mortality rate among young children than any other specific fever, although the public seems scarcely aware of

this. The results of treatment of pertussis and broncho-pneumonia even with penicillin (which should always be given in children aged less than two years) are less satisfactory than in any parallel condition, largely because death so often occurs either from convulsions or from exhaustion consequent upon the incessant bouts of coughing.

VINCENT'S ANGINA

In Vincent's angina, many have claimed good results from the local application of oral penicillin in the form of lozenges or cachets. In severe cases, this method is often a failure and inferior to the results obtained by systemic administration, from which latter method Brockbank (1946) obtained good results. Some still believe organic arsenicals to be the better treatment although, owing to its complete absence of toxicity, systemic penicillin, according to others, would appear to be the drug of choice at present, and it is only fair to add that the use of arsenicals has had vigorous opponents (Jewsbury, 1943). Nevertheless, personal experience with penicillin has been disappointing, and better results have almost always been obtained with the arsenicals.

DIPHTHERIA

For present purposes, diphtheria is considered as non-laryngeal and laryngeal. With regard to "doubtful" throats some people appear to feel quite safe so long as penicillin is being given. It cannot be said too often that penicillin is *never* a substitute for serum. That *C. diphtheriae* is sensitive to penicillin is an undoubted fact, but it is equally true that the damage is done, mainly to the cardiovascular and central nervous systems, by the toxin elaborated from the local lesion. This toxin can be neutralized by antitoxin alone, which is the primary object of treatment. Anything (i.e. penicillin) that will attack the local lesion is merely subsidiary and this must never be forgotten.

Long (1947) has presented "evidence that *C. diphtheriae* can be eliminated in under twenty-four hours in a severe case of diphtheria with a dosage of 1,000,000 units a day", and he regards this as the bare minimum. Karelitz *et al.* (1946), using 120,000 to 240,000 units daily (with antitoxin), found that after five days 27.5 per cent. still showed positive throat cultures as compared with 100 per cent. of the controls. They state that "penicillin was ineffective in preventing toxic complications but seemed to hasten the clearing . . . of complications due to pyogenic organisms". Dee *et al.* (1947) treated 27 early cases with penicillin only, omitting serum. Their paper appears open to criticism, above all for the unjustifiable risk in the omission of antitoxin. Many of their cases were without bacteriological confirmation; nor can the temperature in diphtheria, of all diseases, be regarded as a reliable index of general response to treatment. No temperature is "too high" for diphtheria, and yet again it may be subnormal throughout the illness.

Summarizing then, it appears that penicillin should be given in all cases with secondary infection. In very severe cases with rapidly spreading membrane and bull-neck, in which *intravenous* serum should be given, penicillin in a daily dosage of a million units or more may be of value in

ameliorating the local discomfort by accelerating the disintegration of the membrane. Reduction of the complication rates should not be expected. With mild cases, the fact that rapid disappearance of organisms from the throat is obtained would seem to be the only indication for penicillin. Although this is debatable, perhaps the best course would be to use it only in those patients in whom the development of the convalescent carrier state would appear likely, and in good time before the date of their discharge from hospital. Since the complication rate is unaffected, apart from preventing the development of the carrier state, the general course of the disease, the nursing treatment, and consequently the duration of the period in hospital, are unlikely to be affected, in direct contrast to scarlet fever.

With regard to the *chronic diphtheria carrier*, although oral penicillin is of undoubted value in some cases, Long's method of systemic administration would appear to be much more reliable and may well be the best solution so far found for this ancient problem.

There is extraordinarily little literature on the important subject of *laryngeal diphtheria*, especially in the form that occurs as a late complication of measles. (It must be remembered that this condition always occurs late in measles, usually at the end of the second week; prodromal laryngitis is a simple catarrhal phenomenon.) In a condition that once had a 100 per cent. mortality following tracheotomy, sulphonamides have proved life-saving. Johnstone (1942) published four consecutive cases of recovery and has since then had a further six; ten cases in all. Even for simple laryngeal diphtheria, sulphonamides had a beneficial post-tracheotomy effect in the prevention of subsequent pneumonia, but did nothing towards averting the operation. Penicillin, on the other hand, appears to have a markedly beneficial action in that respect, and since its employment in the Plymouth Isolation Hospital, with one exception, no case of laryngeal diphtheria, out of about ten, has required operation, including cases in which interference would have been almost inevitable in the old days.

The exception occurred in a boy of three admitted as a recovering nasopharyngeal case with secondary laryngeal involvement and unmistakable signs of early broncho-pneumonia. A positive throat swab (type intermedius) was obtained. Despite anti-diphtheria serum, 80,000 units intramuscularly, and penicillin, 40,000 units intramuscularly three-hourly, tracheotomy was required 33 hours after admission. Nine hours later, he suddenly became asphyxiated and died. The tracheotomy tube was patent, but a low tracheal block had occurred due, no doubt, to an extensive diphtheritic broncho-pneumonia.

The aim of chemotherapy in laryngeal diphtheria is twofold: first, if possible, to prevent tracheotomy and, secondly, to prevent the development of secondary pneumonia, particularly after operation. Penicillin administered early enough would appear to achieve both objects, sulphonamides the latter only. Once pneumonia has developed, the prognosis is almost hopeless, and this always used to occur in the cases following measles. The importance of at once giving both penicillin and serum in such cases cannot therefore be overemphasized, and it would be hard to find a more important indication for chemotherapy.

MENINGITIS

Pyogenic meningitis remains for discussion, beginning with *cerebrospinal fever*, the latter perhaps the greatest triumph of all in sulphonamide therapy. Sulphadiazine is the drug of choice, although sulphathiazole is also effective. Banks (1941) in a series of 97 consecutive cases had only two deaths; and in 500 cases of all ages between 1938 and 1942, the total mortality was 6 per cent. Before sulphonamide treatment, the mortality often reached 60 per cent. A curious and insufficiently stressed toxic manifestation of sulphonamide intolerance was first described with sulphapyridine by Johnstone and Forgacs (1941), whereby, despite a cerebrospinal fluid returning to normal, drowsiness, headache and even neck rigidity either return, persist, or get worse. If treatment is continued, death may result, but if the drug is withdrawn the toxic manifestations rapidly disappear. I also have seen this phenomenon with sulphathiazole, but it has not yet been reported after sulphadiazine. This state may have to be distinguished from a meningococcal encephalomyelitis which is fatal (Banks and McCartney, 1942). It is possible, of course, that the two are closely related, and they should, if a case is not going well, be considered as possible but rare causes. The main drawback to the use of penicillin is the necessity for intrathecal administration.

Nevertheless, Rosenberg and Arling (1944), using only penicillin, obtained 65 out of 66 recoveries: "Although one intrathecal injection of 10,000 units controlled some of the milder infections, a minimum of two is advocated. In severe cases as much as five intrathecal injections were required". The sinister fact that meningococci reappeared in four cases out of the 65 must be noted. "One case of Waterhouse-Friderichsen syndrome recovered after 250,000 units systemically in 48 hours". Complications such as acute arthritis and epididymo-orchitis failed to respond (as is the case in gonorrhœa). Meads *et al.* (1945) were much less successful: "The clinical response to penicillin is slower than that to the sulphonamides; abnormal spinal findings persist longer; there may be recurrences, the meningococcus-carrier state may persist; the treatment is difficult, and finally one may have to resort to the sulphonamides for cure". Vengsaker *et al.* (1946) in a larger series confirmed the latter observations, whilst the Department of Health for Scotland (1947) in a small series showed 11 unsuccessful penicillin-treated cases out of 35 as compared with corresponding sulphonamide figures of 5 out of 31. More of the latter group than of the penicillin cases were in infancy and old age (unfavourable age-groups).

In recent correspondence, Banks (1946) has stated:—

"Is it already forgotten that prompt and adequate sulphonamide therapy is rapidly curative in about 95 per cent. of meningococcal cases? Is there any evidence so far that the cure of these can be hastened by penicillin? I do not think so, nor have I any reason to believe that any considerable part of the other five per cent. can be saved by penicillin either".

A quotation from this correspondence (Fluker, 1946b) runs:—

"With the exception of cases of sulphonamide intolerance and those rare cases of the ordinary type of the disease which fail to respond, there is no real indication for the use of penicillin intrathecally in the non-fulminating varieties of cerebrospinal fever. The fulminating cases can be divided perhaps a little arbitrarily into those cases which are often dead within a few hours . . . and the type . . . which progresses to a fatal termination in about twenty-four hours. I have no experience of the use of penicillin in the former type of case, but its efficacy by whatever route

it is administered (and it should certainly be given) would seem doubtful. In the second type of fulminating case, if after a few hours on combined sulphonamide and systemic penicillin therapy the patient's condition is still rapidly deteriorating, then in accordance with the evidence so far available, intrathecal penicillin is indicated . . . Two such injections are usually sufficient. It is important to remember that such cases comprise a very small percentage of the total . . . The immediate risks of intrathecal penicillin are obvious; for example, the introduction of penicillin-resistant organisms—and the possibility of delayed sequelæ such as post-meningitic headache should not be forgotten”.

Two cases illustrating the above types of fulminating cerebrospinal fever are cited (Fluker, 1946c):—

(a) A boy aged ten was playing football at 3 p.m. At 5 p.m. he complained of a sudden and severe headache. At 7 p.m. he was admitted to hospital and, the diagnosis of cerebrospinal fever being confirmed, given intravenous sodium sulphapyridine. At 9 p.m. he was dead. Would penicillin have saved him?

(b) A girl, aged six, was admitted with cerebrospinal fever and a history of eight hours with severe headache and vomiting, for the last three of which she had been comatose and incontinent. On examination she was very ill and had all the classical signs (including Stocker's) together with an extensive purpuric rash. The cerebrospinal fluid contained meningococci. Sulphadiazine was started at once. Eight hours later survival for more than a few hours seemed unlikely. Consequently, penicillin was started at once, 40,000 units intramuscularly three-hourly, and 20,000 units in 20 c.cm. of doubly distilled water given intrathecally. Twenty-four hours later she received a further 15,000 units in 15 c.cm. by this route. Sulphadiazine was withdrawn as penicillin was begun, although one now knows that this was a mistake. Improvement was dramatic and in two days all signs of meningitis had disappeared and she was afebrile. Penicillin was then cut to 30,000 unit doses and continued for a further two days to a total of 950,000 units. An attack first of pyelitis, which responded to sulphathiazole, and later of mild follicular tonsillitis which required no chemotherapy, caused a protracted convalescence, but she was discharged after seven weeks, fit and well.

Penicillin was almost certainly life-saving in this instance, but it must again be emphasized that this type of case is much more severe than the average.

In the correspondence already alluded to, Banks (1946) wrote:—

“In *pneumococcal meningitis*, the balance of evidence at present appears to be in favour of intrathecal and systemic penicillin as well as large doses of sulphonamides. But the evidence for intrathecal penicillin is not so strong as to justify a rush to it without prior examination of a smear from the spinal fluid”.

If facilities for a bacteriological examination of the cerebrospinal fluid are not immediately available, sulphonamides should be used at first and reliance placed upon the subsequent clinical findings. Intrathecal penicillin is better not given in the private house, because of the risk of sepsis, and the maximum dose should never exceed 20,000 units in 20 c.cm. of sterile distilled water, as with quantities much in excess of this instances of aseptic meningitis, and even of severe cerebral reactions, have been reported (Cairns, 1944; Sweet *et al.*, 1945).

Honor Smith *et al.* (1946) published a series of 38 cases. Of these, the last eighteen, all of which recovered, received intrathecal and systemic penicillin with sulphadiazine by mouth as follows:—“Once pneumococci are seen, a lumbar injection of 8000-16,000 units of penicillin is given” (appropriately less for infants). “Systemic penicillin is begun . . . and 120,000 units is given in 24 hours”. Sulphadiazine was given, 2 gm. four-hourly for 4-5 days, and then 1 gm. four-hourly up to the end of the week to cover the period of withdrawal of the penicillin. A second intrathecal injection is recommended within twelve to eighteen hours and thereafter one a day, a minimum of five such injections being given.

MENINGITIS

Pyogenic meningitis remains for discussion, beginning with *cerebrospinal fever*, the latter perhaps the greatest triumph of all in sulphonamide therapy. Sulphadiazine is the drug of choice, although sulphathiazole is also effective. Banks (1941) in a series of 97 consecutive cases had only two deaths; and in 500 cases of all ages between 1938 and 1942, the total mortality was 6 per cent. Before sulphonamide treatment, the mortality often reached 60 per cent. A curious and insufficiently stressed toxic manifestation of sulphonamide intolerance was first described with sulphapyridine by Johnstone and Forgacs (1941), whereby, despite a cerebrospinal fluid returning to normal, drowsiness, headache and even neck rigidity either return, persist, or get worse. If treatment is continued, death may result, but if the drug is withdrawn the toxic manifestations rapidly disappear. I also have seen this phenomenon with sulphathiazole, but it has not yet been reported after sulphadiazine. This state may have to be distinguished from a meningococcal encephalomyelitis which is fatal (Banks and McCartney, 1942). It is possible, of course, that the two are closely related, and they should, if a case is not going well, be considered as possible but rare causes. The main drawback to the use of penicillin is the necessity for intrathecal administration.

Nevertheless, Rosenberg and Arling (1944), using only penicillin, obtained 65 out of 66 recoveries; "Although one intrathecal injection of 10,000 units controlled some of the milder infections, a minimum of two is advocated. In severe cases as much as five intrathecal injections were required". The sinister fact that meningococci reappeared in four cases out of the 65 must be noted. "One case of Waterhouse-Friderichsen syndrome recovered after 250,000 units systemically in 48 hours". Complications such as acute arthritis and epididymo-orchitis failed to respond (as is the case in gonorrhœa). Meads *et al.* (1945) were much less successful: "The clinical response to penicillin is slower than that to the sulphonamides; abnormal spinal findings persist longer; there may be recurrences, the meningococcus-carrier state may persist; the treatment is difficult, and finally one may have to resort to the sulphonamides for cure". Vengsarker *et al.* (1946) in a larger series confirmed the latter observations, whilst the Department of Health for Scotland (1947) in a small series showed 11 unsuccessful penicillin-treated cases out of 35 as compared with corresponding sulphonamide figures of 5 out of 31. More of the latter group than of the penicillin cases were in infancy and old age (unfavourable age-groups).

In recent correspondence, Banks (1946) has stated:—

"Is it already forgotten that prompt and adequate sulphonamide therapy is rapidly curative in about 95 per cent. of meningococcal cases? Is there any evidence so far that the cure of these can be hastened by penicillin? I do not think so, nor have I any reason to believe that any considerable part of the other five per cent. can be saved by penicillin either".

A quotation from this correspondence (Fluker, 1946b) runs:—

"With the exception of cases of sulphonamide intolerance and those rare cases of the ordinary type of the disease which fail to respond, there is no real indication for the use of penicillin intrathecally in the non-fulminating varieties of cerebrospinal fever. The fulminating cases can be divided perhaps a little arbitrarily into those cases which are often dead within a few hours . . . and the type . . . which progresses to a fatal termination in about twenty-four hours. I have no experience of the use of penicillin in the former type of case, but its efficacy by whatever route

PHARYNGEAL ABSCESSSES IN YOUNG CHILDREN

By F. BOYES KORKIS, M.B., F.R.C.S.Ed., D.L.O.

Surgeon, Metropolitan Ear, Nose and Throat Hospital, London.

In young children, abscesses of the pharynx and fauces, secondary to acute infections of the pharyngeal structures, fall into two main groups, being either retropharyngeal or peritonsillar in situation.

(1) *Retropharyngeal abscess*.—This condition arises as a suppurative adenitis of those lymphatic glands which are found in the retropharyngeal fascial space, between the constrictor muscles of the pharynx in front, and the pre-vertebral fascia behind. This space is limited medially by the buccopharyngeal fascia, which binds the middle line of the back of the pharynx firmly to the pre-vertebral fascia (Lee McGregor, 1936). Hence an abscess resulting from the breakdown of the retropharyngeal lymph glands is always to one side of the middle line, and is never central in position. This fact is of clinical significance in that it serves to differentiate the acute type of retropharyngeal abscess from the chronic. The swelling resulting from a chronic abscess, caused by tuberculous caries of the cervical vertebræ, is in the midline of the pharynx, the pus lying *behind* the pre-vertebral fascia.

(2) *Peritonsillar abscess*.—The collection of pus is situated between the tonsil medially and the constrictors of the pharynx laterally, the usual type arising as a result of infection of a superior crypt, the base of which is in contact with the fibrous tissue of the capsule near the superior pole of the tonsil (Brighton, 1942). Penetration of the pus through the superior constrictor muscle may take place, resulting in a secondary abscess of the parapharyngeal space.

REPORTS OF TWO CASES

These cases are reported as examples of pharyngeal abscesses in children of an unusual age, in order to serve as a basis for some comments which will be made later.

Case No. 1.—S.H., female, two-and-a-half years of age, admitted to hospital on December 23, 1946, with a history of sore throat and malaise for one week. On examination the following day the temperature was 101° F. (38.3° C.), the breathing was difficult, slight cyanosis was present, and marked fœtor oris. A large left-sided peritonsillar abscess partially blocked the airway, and the upper deep cervical glands were palpable and tender. The abscess was incised forthwith and a large quantity of thick pus was evacuated. The general condition improved rapidly. On December 25 the temperature was normal, and four days later the peritonsillar swelling had completely subsided and the adenitis had settled. The patient was discharged on the following day. Bacteriological examination of the throat swab showed *M. catarrhalis*, non-hæmolytic streptococci, and hæmolytic streptococci. The pus from the quinsy grew mixed organisms, chiefly *Staph. aureus*. There were no Klebs-Lœffler bacilli demonstrated in either swab.

If the cerebrospinal pathways become blocked, intraventricular penicillin injections are indicated. The most reliable sign of impending block is difficulty in obtaining fluid on lumbar puncture, with the subsequent development of an abnormal Queckenstedt test. The fluid generally becomes thicker but is sometimes crystal clear. At this stage, Shalom (1945) suggests the intravenous administration of hypertonic solutions, but if these are without apparent effect, the ventricles should be tapped and penicillin given by that route if a block is shown to be present. (This is determined apart from clinical signs, by a penicillin assay of the intraventricular fluid following the previous administration of the drug by the lumbar route.) The decision to undertake these drastic measures should rest with those possessed of considerable experience of this type of malady and the services of a neurosurgeon should be obtained whenever possible. Finally, attention to the frequently causal focal sepsis, e.g. otitis media, may be required when the meningitis appears to be controlled, as this type of meningitis is prone to relapse. Every case must be treated on its own merits as is well exemplified by the following case (Fluker, 1946c):—

A girl, aged three, was admitted with a right lower lobe pneumonia and pneumococcal meningitis. She had been ill for ten days and had received sulphadiazine, $\frac{1}{2}$ gm. for a week (= 21 gm.). Three days before admission, she had developed signs of meningitis. Following lumbar puncture, a diagnosis of pneumococcal meningitis had been confirmed, following which she had received a further 6 gm. of sulphadiazine, and penicillin 6000 units intrathecally. In view of the previous and prolonged administration of sulphadiazine, penicillin alone was given, 40,000 units intramuscularly three-hourly, and 20,000 units intrathecally. The next day she was much better and 10,000 units were given by the lumbar route. On the third day she was less well, and neck rigidity with a positive Kernig's sign was much more marked. The cerebrospinal fluid was perfectly clear under normal pressure, with a normal Queckenstedt and sterile. The fourth intrathecal injection, this time of 4000 units, was given and sulphadiazine restarted. Late that night she was still worse although there was no evidence of any block in the cerebrospinal pathways. To make matters worse she had an acute myocarditis. The meningeal irritation was therefore considered to be the result of the penicillin, or even a toxic manifestation of sulphadiazine (*vide supra*) which was withdrawn, only systemic penicillin being continued. Although her cardiac condition caused anxiety for some time, after twenty-four hours all neck rigidity had disappeared. Intramuscular penicillin was continued for a further two days to a total of 1,600,000 units, and after being nursed flat (on one pillow) for a week, she made a rapid and permanent recovery, being discharged five weeks after admission.

This case has been quoted because it caused much anxiety at the time and illustrates the difficulties in management which may arise.

In conclusion, a brief reference to the meningitis caused by *Hæmophilus influenzae* is worth while. Sulphadiazine is, according to Illingworth (1945), the treatment of choice, combined, in appropriate cases, with the anti-influenzal type B rabbit antiserum. Streptomycin is effective in moderate, but not in severe cases. In the absence of serum or streptomycin, penicillin in combination with sulphadiazine is recommended, as with pneumococcal meningitis.

The references to this article are obtainable on application to the Editor.

PHARYNGEAL ABSCESSSES IN YOUNG CHILDREN

By F. BOYES KORKIS, M.B., F.R.C.S.Ed., D.L.O.

Surgeon, Metropolitan Ear, Nose and Throat Hospital, London.

In young children, abscesses of the pharynx and fauces, secondary to acute infections of the pharyngeal structures, fall into two main groups, being either retropharyngeal or peritonsillar in situation.

(1) *Retropharyngeal abscess*.—This condition arises as a suppurative adenitis of those lymphatic glands which are found in the retropharyngeal fascial space, between the constrictor muscles of the pharynx in front, and the pre-vertebral fascia behind. This space is limited medially by the buccopharyngeal fascia, which binds the middle line of the back of the pharynx firmly to the pre-vertebral fascia (Lee McGregor, 1936). Hence an abscess resulting from the breakdown of the retropharyngeal lymph glands is always to one side of the middle line, and is never central in position. This fact is of clinical significance in that it serves to differentiate the acute type of retropharyngeal abscess from the chronic. The swelling resulting from a chronic abscess, caused by tuberculous caries of the cervical vertebræ, is in the midline of the pharynx, the pus lying *behind* the pre-vertebral fascia.

(2) *Peritonsillar abscess*.—The collection of pus is situated between the tonsil medially and the constrictors of the pharynx laterally, the usual type arising as a result of infection of a superior crypt, the base of which is in contact with the fibrous tissue of the capsule near the superior pole of the tonsil (Brighton, 1942). Penetration of the pus through the superior constrictor muscle may take place, resulting in a secondary abscess of the parapharyngeal space.

REPORTS OF TWO CASES

These cases are reported as examples of pharyngeal abscesses in children of an unusual age, in order to serve as a basis for some comments which will be made later.

Case No. 1.—S.H., female, two-and-a-half years of age, admitted to hospital on December 23, 1946, with a history of sore throat and malaise for one week. On examination the following day the temperature was 101° F. (38.3° C.), the breathing was difficult, slight cyanosis was present, and marked fœtor oris. A large left-sided peritonsillar abscess partially blocked the airway, and the upper deep cervical glands were palpable and tender. The abscess was incised forthwith and a large quantity of thick pus was evacuated. The general condition improved rapidly. On December 25 the temperature was normal, and four days later the peritonsillar swelling had completely subsided and the adenitis had settled. The patient was discharged on the following day. Bacteriological examination of the throat swab showed *M. catarrhalis*, non-hæmolytic streptococci, and hæmolytic streptococci. The pus from the quinsy grew mixed organisms, chiefly *Staph. aureus*. There were no Klebs-Löffler bacilli demonstrated in either swab.

If the cerebrospinal pathways become blocked, intraventricular penicillin injections are indicated. The most reliable sign of impending block is difficulty in obtaining fluid on lumbar puncture, with the subsequent development of an abnormal Queckenstedt test. The fluid generally becomes thicker but is sometimes crystal clear. At this stage, Shalom (1945) suggests the intravenous administration of hypertonic solutions, but if these are without apparent effect, the ventricles should be tapped and penicillin given by that route if a block is shown to be present. (This is determined apart from clinical signs, by a penicillin assay of the intraventricular fluid following the previous administration of the drug by the lumbar route.) The decision to undertake these drastic measures should rest with those possessed of considerable experience of this type of malady and the services of a neurosurgeon should be obtained whenever possible. Finally, attention to the frequently causal focal sepsis, e.g. otitis media, may be required when the meningitis appears to be controlled, as this type of meningitis is prone to relapse. Every case must be treated on its own merits as is well exemplified by the following case (Fluker, 1946c):—

A girl, aged three, was admitted with a right lower lobe pneumonia and pneumococcal meningitis. She had been ill for ten days and had received sulphadiazine, $\frac{1}{2}$ gm. for a week (≈ 21 gm.). Three days before admission, she had developed signs of meningitis. Following lumbar puncture, a diagnosis of pneumococcal meningitis had been confirmed, following which she had received a further 6 gm. of sulphadiazine, and penicillin 6000 units intrathecally. In view of the previous and prolonged administration of sulphadiazine, penicillin alone was given, 40,000 units intramuscularly three-hourly, and 20,000 units intrathecally. The next day she was much better and 10,000 units were given by the lumbar route. On the third day she was less well, and neck rigidity with a positive Kernig's sign was much more marked. The cerebrospinal fluid was perfectly clear under normal pressure, with a normal Queckenstedt and sterile. The fourth intrathecal injection, this time of 4000 units, was given and sulphadiazine restarted. Late that night she was still worse although there was no evidence of any block in the cerebrospinal pathways. To make matters worse she had an acute myocarditis. The meningeal irritation was therefore considered to be the result of the penicillin, or even a toxic manifestation of sulphadiazine (*vide supra*) which was withdrawn, only systemic penicillin being continued. Although her cardiac condition caused anxiety for some time, after twenty-four hours all neck rigidity had disappeared. Intramuscular penicillin was continued for a further two days to a total of 1,600,000 units, and after being nursed flat (on one pillow) for a week, she made a rapid and permanent recovery, being discharged five weeks after admission.

This case has been quoted because it caused much anxiety at the time and illustrates the difficulties in management which may arise.

In conclusion, a brief reference to the meningitis caused by *Hæmophilus influenzae* is worth while. Sulphadiazine is, according to Illingworth (1945), the treatment of choice, combined, in appropriate cases, with the anti-influenzal type B rabbit antiserum. Streptomycin is effective in moderate, but not in severe cases. In the absence of serum or streptomycin, penicillin in combination with sulphadiazine is recommended, as with pneumococcal meningitis.

The references to this article are obtainable on application to the Editor.

obtaining satisfactory illumination of the area under examination, in domiciliary practice, are contributory factors responsible for the error in diagnosis.

If these causes of cyanosis and respiratory obstruction in young children are borne in mind, a careful examination of the pharynx with a good light should enable the correct diagnosis to be made. The presence of a marked, unilateral and painful enlargement of the upper deep cervical glands is a helpful sign in those cases in which a clear view of the pharynx is unobtainable owing to trismus. A correct diagnosis was made before admission in the case of peritonsillar abscess reported, but the presence of a retro-pharyngeal collection was undetected before specialist examination in the other case, the diagnosis of "recurrent tonsillitis" being formulated.

Treatment.—Rapid recovery follows the evacuation of the pus, as in the case reported by Comtry and Shun-Shin (1936). This was found to be so in the cases reported here.

The incision of the abscess can be carried out either with or without an anæsthetic. An adequate exposure of the field and an adequate incision are essential, and for this reason I prefer the use of a general anæsthetic if circumstances and the patient's general condition permit. There is little danger of the inhalation of blood and pus if the operation is carried out in the tonsillar position, with the head and neck extended by means of a sandbag placed beneath the shoulders, if use is made of a suitable mouth gag (such as the Boyle-Davis), and if a suction apparatus is at hand. The danger is still further lessened if the depth of the anæsthesia is such that the pharyngeal and cough reflexes are just returning at the time the incision is made.

Both the cases reported here were managed in this manner. Aspiration of the pus before incision was not carried out, as both abscesses were fluctuant, and it was evident that pus was present. Some surgeons make it their practice to aspirate before drainage of the abscess: Cone (1945) suggests that aspiration permits earlier localization and drainage of the collection of pus; Maclean (1935) also confirms the presence of pus by aspiration before incision.

In this age of *chemotherapeutic treatment*, it might well be asked what place the sulphonamides and penicillin hold in treatment. By their use, cases which are seen early, before there is actual formation of pus, may be aborted, but once an abscess has formed, surgical drainage is called for, and their rôle becomes supportive only. Rosenberg (1946) believes that penicillin therapy helps to prevent peritonsillar abscess formation in cases of peritonsillitis, but he incises and drains the abscess once it has formed.

Bacteriology.—The organisms recovered from these abscesses are usually of the pyogenic group, but mixed infections are common, and *M. catarrhalis* is often recovered. The diphtheria bacillus was not found in any of the cases reviewed, but there appears to be no reason why it should not occur in combination with a pyogenic infection, and a routine throat swab should be taken to exclude this infection. In the two cases reported a mixed infection was present.

Case No. 2.—N.S., male, aged two-and-a-half years, was seen on May 26, 1947, with a history of sore throat and malaise for two weeks. An exacerbation of the pain had been noted for one week. On examination the temperature was 102° F. (38.9° C.). The upper deep cervical glands were enlarged and tender on the left side. There was a small tonsillar gland, non-tender, on the right side. A fluctuant swelling was present on the left side of the posterior pharyngeal wall, extending from the level of the soft palate superiorly, to a point below the level of the tongue.

Under a general anæsthetic the swelling was seen to extend down to the level of the epiglottis. Incision released a large amount of thick pus. Convalescence was rapid and uneventful, the adenitis subsiding in three days and the child returning home on the fourth. No Klebs-Löffler bacilli were found on bacteriological examination. There was a heavy growth of hæmolytic streptococci, with some diphtheroids and *M. catarrhalis* on culture.

DISCUSSION

Age incidence.—It is stated by Shambaugh (1945) that in older children the retropharyngeal lymph nodes have usually disappeared, so that acute retropharyngeal abscess is a disease of infancy, more than half the cases occurring in the first year of life. Ballenger (1947), quoting Babbitt, records 66 per cent. of cases arising in the first year of life. Acute retropharyngeal abscess is an uncommon condition. Faier (1933) found a total of 155 cases out of 88,849 admissions to children's hospitals. It is usually considered that peritonsillar abscess, although a common clinical entity, is rare in children. Ballenger (1947) states that "the disease is common in young adults but rare in children". Brighton (1942) remarks that "simple peritonsillar abscess occurs most frequently between the ages of fifteen and forty. It is rarely found in early childhood". Scott Stevenson (1938) writes that the condition is relatively rare in children. "The affection is rare in children and is commonest in adult males", says Logan Turner (1932). Turning to detailed reports of published cases, these comments are confirmed. Salingre (1938) records 54 cases, the ages varying from three to forty-eight years. Capus (1943) reports a series of 33 cases, the age variation being from three to fifty-three years. Weeth (1937) states that in young children peritonsillitis usually subsides without the formation of pus, an explanation which would account for the comparative rarity of this condition in infancy. Both cases recorded here were aged two-and-a-half years, which is young for peritonsillar abscess and somewhat old for retropharyngeal abscess.

Diagnosis.—Most authors refer to the difficulty of diagnosis, a misdiagnosis often being made before admission to hospital. Thus, Maclean (1935), in his first case, notes that the child was sent to hospital as a case of diphtheritic croup, and he states that these patients are usually regarded by their doctors as suffering from diphtheria. This is readily understandable in view of the fact that these infants cannot draw attention to their symptoms, and, in addition, often present a striking clinical picture of respiratory obstruction, with epibarrassment to the breathing, head and rib retraction, and sometimes slight cyanosis. Moreover, the inability to obtain a good view of the pharynx due to trismus, and the difficulty of

THE RÔLE OF BISMUTH OXYCHLORIDE IN THE TREATMENT OF SYPHILIS

By R. R. WILLCOX, M.B., B.S., M.R.C.S.

Physician in Charge, Venereal Diseases Department, King Edward VII Hospital, Windsor; Senior Assistant, Venereal Diseases Department, St. Mary's Hospital, London; Formerly Adviser in Venereology to the War Office.

BISMUTH still has an undisputed place as an adjuvant in the treatment of late syphilis, and it is also widely used in conjunction with penicillin and the arsenical drugs in early syphilis.

EARLY SYPHILIS

Before the discovery of penicillin, bismuth provided the background while the hammer blows of neoarsphenamine were, with suitable intervals, administered for a year. Just before the 1939-45 war, efforts were made to intensify the treatment by employing the arsenoxides (mapharsen) for periods of five, eight and twenty days, or for longer periods up to twelve or twenty-six weeks. With all of these schedules it was found that good results were forthcoming only if the additive agent of bismuth was retained. The introduction of penicillin necessitated a complete readjustment of ideas for, if neoarsphenamine was a hammer, penicillin proved by comparison to be a pile-driver, as it frequently achieved in a week what with older treatments required a year. However, a later assessment showed a failure rate of up to 25-35 per cent. when early syphilis was treated with penicillin alone; although better results, as yet unpublished, are hoped from crystalline penicillin G, which has so far enjoyed two years' widespread use in the treatment of syphilis in the United States.

Crystalline penicillin G is only just becoming available in this country and the interim period has been occupied, both in the Armed Services and most civilian clinics, by combining a course of not less than 4.0 to 4.8 million units of penicillin (using in the main oil-beeswax preparations, with not less than eight single daily injections) plus bismuth and arsenic, usually given as weekly injections of both drugs for ten weeks. Time may yet show that the arsenic and even the bismuth may be omitted, but as the latter is not a highly toxic drug, its use combined with penicillin may continue. It remains a particular favourite of the French school.

LATE SYPHILIS

Bismuth is still indicated for the treatment of late syphilis as a means of avoiding the unpleasant reactions of *therapeutic shock* and *therapeutic paradox*. A local Jarisch-Herxheimer reaction at the site of disease may

Prognosis.—With proper management this is usually good. The most likely complication, especially in children, is otitis media. The possibility of death from asphyxiation following the spontaneous rupture of an abscess or of septic lung complications, makes surgical intervention necessary. Spread of infection to the deep structures of the neck, lateral to the constrictor muscles, is a serious complication, but adequate chemotherapy should reduce the incidence of this extension. Beck (1947) states that severe, and often fatal, hæmorrhage may result from the erosion of arteries in these parapharyngeal space infections. Downward spread of infection to the mediastinum is also known, and Richtner (1946) considers that this is more likely to follow retropharyngeal abscess than quinsy, as the pre-vertebral space constitutes a part of the posterior mediastinum. The prognosis in these cases is grave. Owing to the age incidence of retropharyngeal abscess this dreaded complication is more likely to occur in children.

CONCLUSIONS

- (1) An outline is given of the applied anatomy and pathology relating to retropharyngeal and peritonsillar abscess.
- (2) The literature relating to these conditions in children is reviewed.
- (3) An example of each condition, encountered in my practice, is given to serve as a basis for discussion.
- (4) Treatment is discussed. There is ample evidence that incision and drainage should be carried out once the abscess has localized, whether or not chemotherapy has been employed as an adjunct in treatment.

References

- Ballenger, W. L., and H. C. (1947): "Diseases of the 'Throat, Nose and Ear,' 9th edition, London, pp. 282, 332.
- Beck, A. L. (1947): *Ann. Oto-laryng.*, **56**, 439.
- Berman, H. L. (1934): *Arch. Otolaryng.*, *Chicago*, **19**, 710.
- Brighton, G. R. (1942): "Surgery of the Nose and Throat," New York, p. 281.
- Capus, B. (1943): *Arch. Otolaryng.*, *Chicago*, **38**, 210.
- Comtry, R., and Shun-Shin, M. (1936): *Brit. med. J.*, **i**, 1207.
- Cone, A. J. (1945): *Ann. Oto-laryng.*, **54**, 84.
- Faier, S. Z., (1933): *Ibid.*, **42**, 408.
- Maclean, A. (1935): *Brit. med. J.*, **ii**, 254.
- McGregor, A. L. (1936): "Synopsis of Surgical Anatomy," 4th edition, Bristol, p. 183.
- Richtner, N. G. (1946): *Acta otolaryng.*, *Stockh.*, **34**, 521.
- Rosenberg, A. (1946): *Arch. Otolaryng.*, *Chicago*, **44**, 662.
- Salingre, E. (1938): *Acta otolaryng.*, *Stockh.*, **26**, 734.
- Shambaugh, G. E., Jun. (1945): "Diseases of the Nose Throat and Ear," (edited by C. and C. L. Jackson), Philadelphia, p. 151.
- Stevenson, R. Scott (1938): *Brit. med. J.*, **i**, 1323.
- Turner, A. Logan (1932): "Diseases of the Nose, Throat and Ear," 3rd edition, Bristol, p. 132.
- Weeth, C. R. (1937): *Amer. J. Surg.*, **36**, 161.

AFRICAN MEDICINE

By WILLIAM A. R. THOMSON, M.D.

THIS flying business certainly strains one's powers of adaptation, but on the other hand its advantages far outweigh its disadvantages. For instance, to leave London on a miserable gray morning in January, have afternoon tea the same day at Marseilles, dine that evening at Malta, sample El Adem and the torrid heat of the desert the following afternoon and spend the night at Cairo is an experience which even the seasoned flyer never forgets. As a means of studying the scenery it is a poor substitute for surface travel, but as a means of satisfying the modern urge for seeing the maximum amount of the world in the minimum of time it is supreme. The experience of being able to make a tour of Africa extending from Cairo to the Cape within a period of two months, is only possible because of the air travel facilities available, and whilst it is clearly impossible to obtain more than superficial impressions in such a short space of time, the mere speed of the tour did serve to give a vivid impression of the general picture of medical practice in the areas visited.

SOME GENERAL IMPRESSIONS

The predominant impression left upon one's mind is of the tremendous problems involved and of the excellent manner in which these are being tackled by a service which is sadly lacking in both manpower and money. The members of the Colonial Medical Service are doing a first-class job of work, and the fact that there is still so much to be done is no fault of theirs. Rather is it a case of so much having been done by so few. Indeed the Service might take as their motto the historic words of an historic statesman: "Give us the tools and we shall finish the job". What most impresses the visitor to Africa is how little is known concerning the incidence of disease. Men and money have never been available to allow of systematic surveys such as are now considered essential in any well-run state. Morbidity statistics based upon hospital returns are always notoriously unreliable, and this is particularly true in Africa, where follow-up is almost impossible and where patients are all too liable to walk out of hospital within two days of admission, simply because they feel better! As an example of how deficient is our information, it is only at the present moment that the first systematic survey of the incidence of leprosy in East Africa is being carried out—and this is being done (most efficiently, let it be added) by one man!

Then again, little is known about the nutritional status of the native. Much is talked about malnutrition, but the data upon which to base dogmatic statements do not exist. That malnutrition exists no one could deny, but the real extent and nature is still unknown. For instance, even such a carefully investigated subject as the nutritional anæmias is still

follow precipitate treatment with arsenic or penicillin (therapeutic shock), although in cardiovascular syphilis, at any rate, this risk is much reduced with penicillin. Such local flare-ups usually do no harm but in certain cases, such as aortitis involving the coronary ostia, gummas of the larynx, optic atrophy, and syphilitic meningitis, to name but a few, this process may invoke a sudden intensification of the lesions, causing more severe and perhaps permanent damage, and even death. A too rapid involution of a gummatous liver, a syphilitic aorta or of the diseased brain of a parietic may produce a therapeutic paradox. Although satisfactory healing may occur, the tissue distortion which may arise from the fibrotic process can result in ascites, cardiac decompensation or mental deterioration, respectively, in each of the three examples quoted. These risks may be lessened if bismuth is given for a preliminary period of four to eight weeks before penicillin or the arsenical drugs are employed.

Most clinicians also consider that, if penicillin alone fails in a not negligible proportion of early syphilitics, it is asking too much to expect greater success in the essentially chronic disease of late syphilis. Thus, in addition to penicillin, at least two courses of either bismuth alone or arsenic and bismuth are advised. Each course should consist of ten weekly injections.

CONGENITAL SYPHILIS

Bismuth in proportionate doses is likewise combined with penicillin in the treatment of both early and late congenital syphilis. The same considerations apply as in early and late acquired syphilis in the adult, although, if adjuvant treatment is given to the penicillin-treated syphilitic infant, many will employ two full ten-week courses of both sulpharsphenamine *and* bismuth.

THE PREPARATION OF CHOICE

Bismuth subsalicylate suspensions in oil are generally favoured in the United States. In this country aqueous suspensions of bismuth metal or bismuth oxychloride are preferred, it being felt that the results obtained with the three substances do not greatly differ and that the oxychloride is acceptable for general purposes. It is usually supplied in 10 or 20 per cent. suspensions, containing the equivalent of 0.08 and 0.16 gm. of bismuth metal, respectively: 2 c.cm. of the 10 per cent. and 1 c.cm. of the 20 per cent. suspension may be injected intramuscularly, once or twice each week.

in Africa, it must be confessed that up to date little has been done by the authorities to implement this in practice. Too often one visited laboratories normally designated for research purposes, but in which practically the entire staff and facilities were inundated with routine work which had gradually accumulated over a period of years, until research of any quality was wellnigh impossible. Again, no blame can be attached to the staff. Indeed no one is more outspoken than they in deprecating this state of affairs. Two notable exceptions to this unfortunate state of affairs stand out in my memories of a memorable tour.

First must be mentioned the *Yellow Fever Research Institute* at Entebbe in Uganda. Situated on the hills overlooking Lake Victoria, this must be one of the most efficiently organized research institutes in Africa. Organized and run by the Rockefeller Foundation, it had the great good fortune to have as its first director a Canadian whose name is now a household word wherever research work into yellow fever is being carried out. Dr. A. F. Mahaffy's successor in the directorship—Dr. K. C. Smithburn—is worthily maintaining the high traditions of his predecessor. The standard of equipment of the laboratory is only equalled by the quality of the work that is being done both in the Institute and in the field station situated out in the west of Uganda. In the course of the work on yellow fever, several new viruses have been discovered which may well be found to play an important part in the etiology of some of the obscure neurological conditions which are found among the natives. In addition to much valuable information on viruses, the thoroughness with which the work is being done is resulting in the accumulation of a mass of data concerning mosquitoes and monkeys. This Institute is shortly being handed over by the Rockefeller Foundation to the Colonial Office, and it is to be hoped that under its new control the same high standard of efficiency, originality and enthusiasm will be maintained.

The other outstanding example of carefully coordinated research work was that being done on *bilharzia* in Southern Rhodesia. Bilharzia is one of the major public health problems in this most attractive colony, and I was most impressed with the thoroughness with which the problem is being tackled. The problem is far from solved, either from the curative or the preventive aspect, but the work in Southern Rhodesia has been so carefully planned and supervised that it will be a permanent contribution to the ultimate solution of a problem which is by no means confined to this country. This is the home of the intensive antimonial treatment of the disease, but this is merely one facet of the work. Impressive though the results are of this form of treatment, it is clearly not the final answer to the problem. In the hands of its originators the toxic complications have not been serious, but there is little doubt that in less capable hands this is a form of treatment with many hazards.

wrapped in mystery so far as etiology is concerned. Much has been written on this subject, many different views have been advanced as to causation but in none of the colonies which I visited did there appear to exist a hospital with a suitable ward into which patients with nutritional deficiencies could be placed for full and careful clinical, hæmatological and biochemical investigation. A beginning has been made at the Mulago Hospital, Kampala, but the facilities are wholly inadequate, and not because of lack of keenness on the part of the medical personnel but simply because neither men nor means are available. An even more fundamental defect in the problem of nutrition is that so little is known concerning the nutritional status and the physiology of the "normal" native. And one came away wondering, as many others have done before, whether in their enthusiasm certain nutritional experts were not drawing invalid conclusions on the subject of the nutritional status of the natives simply because they were using the European as their yardstick.

HOSPITALS

To the visitor from the United Kingdom, perhaps one of the most vivid impressions of Africa is the congested state of the hospitals. To be informed, quite casually, by a D.M.S. that during the current year the number of patients per bed at any one time averaged $1\frac{1}{2}$ makes the visitor realize with a bump that he really has left British standards behind him. And to visit a native hospital and see anything up to three patients in one bed, with quite a number of convalescent patients sleeping on palliasses on the floor in between beds, leaves a memory that one visitor at least is likely to forget. Once again, the men on the spot must not be blamed, once again it must not be forgotten that British standards are not necessarily the same as those applicable in Africa. The present congestion is partly due to the inevitable hold-up of building during the war, which has struck the East African colonies almost as badly as it has Great Britain. It is also due to the rapidly increasing popularity of hospital treatment among natives. Whereas, even twenty years ago, it was with the utmost difficulty that natives could be compelled to enter hospital for treatment, to-day the difficulty is in persuading them that admission to hospital is not necessary. This increasing popularity of the hospitals, although temporarily embarrassing, is a striking indication of the success of the Medical Service, and I was interested to learn in one colony that the women in the maternity unit had not only acceded to, but even welcomed, the proposal that their infants should be housed in a separate crèche in the hospital and only brought to the mothers for feeding.

RESEARCH FACILITIES

Although in the past much lip-service has been paid to medical research

amœbic dysentery. The major problem here would appear to be adequate control of the acute phase. Emetine is not the last word. It may control the acute form but it cannot be depended upon to cure it, and there is no known remedy which is satisfactory in the treatment of the chronic form. There would appear to be little doubt that a new approach to the problem is necessary and that some fundamental work is required upon the metabolic processes of the amœba to try and discover some preparation which will prove to be a really effective amœbicide.

Tuberculosis.—In practically every area of East and South Africa tuberculosis constitutes a major problem. The condition is so rife that it has so far proved impossible to inaugurate a systematic attack. Whilst the disease usually assumes an acute form, there is some data accumulating which suggests that the more chronic forms are not as rare as is sometimes suggested. The attack here must clearly be twofold: preventive and curative. The former is predominantly a social problem, but no matter how rapidly the living conditions of the native are improved, there will still be ample scope for curative methods. Streptomycin is an obvious weapon here, but the problem is such a vast one that the financial aspects of streptomycin will, for a long time, prove a brake upon its widespread use. On the other hand, there is obvious scope in East Africa for large-scale clinical trials of this antibiotic. Unfortunately I did not have the opportunity of visiting the excellent dispensary organization for the control of tuberculosis which is being carried out on the slopes of Kilimanjaro.

Leprosy.—At long last adequate steps are being taken to bring this historic disease under control. As an essential preliminary, a survey is being made of the incidence of the disease in the East African colonies, a survey which is revealing the vast extent of the problem. Fortunately, the initial results with the newer anti-leprosy preparations, such as diasone and sulphetrone, are promising. In a chronic disease such as leprosy, it is impossible to assess the true value of a remedy until it has been used in a large number of cases over a long period of time, but even the most cautious and most experienced of workers are optimistic. Neither of these preparations is the final answer to this age-long problem, but the results with sulphetrone suggest that it should not be too long before organized research can produce a really effective remedy.

THE OUTLOOK FOR MEDICAL PRACTICE

In these days, medical practitioners, like many other sections of the community, are seriously considering the possibilities of emigration to various parts of the Commonwealth and Empire. To dogmatize is always dangerous, but the following is an attempt to summarize the prospects as they seemed to one visitor. In East Africa, i.e. Kenya, Uganda and Tanganyika, there is little further scope at the moment in private practice. Even in Nairobi, with its relatively large white population, there is really no room for more

SOME COMMON DISEASES

Malaria.—Disappointingly little information was available concerning the relative values of mepacrine and paludrine in prophylaxis. From a mass of contradictory "clinical impressions", the one definite fact that did appear was that whatever the final conclusion might be concerning these two potent preparations, a tablet of paludrine per week would not be the adequate prophylactic dose that it so dramatically proved to be in New Guinea. But what is clearly necessary is a large-scale, carefully controlled investigation of the effect of both these preparations. Of the relative non-toxicity of paludrine, there appeared to be little doubt. One interprising medical officer, for instance, had taken up to ten tablets in one day with impunity! From the curative point of view, the general consensus of opinion was that quinine should be given for the first twenty-four hours, as it controlled the condition more rapidly than any other drug, and that subsequently mepacrine should be given. In the case of adult natives, there were some who believed that, unless it was a severe infection, it was unwise to treat the condition too energetically with any of the antimalarial preparations, as there was some risk in so doing of interfering with the acquired immunity of the patient.

Sleeping sickness.—There is still no effective remedy for the control of infections with *T. rhodesiense*. Cases due to *T. gambiense* respond fairly well to antrypol or suramin if given early enough, but these preparations are of doubtful efficacy in cases due to *T. rhodesiense*. Opinions differed as to the value of tryparsamide. In some areas its use had practically been given up because of its toxicity. There appeared to be considerable difference of opinion as to whether the blindness, which is so liable to develop in these cases, was due to the disease or to the tryparsamide. A certain amount of interest was being evinced in the possible prophylactic value of pentamidine.

Schistosomiasis.—This constitutes one of the major medical problems in Africa, particularly in Egypt, Southern Rhodesia and South Africa. Its gradual spread throughout South Africa is one of the noteworthy features of recent years. From the therapeutic angle, some excellent work is being done in Southern Rhodesia, the home of the intensive antimonial treatment of the disease. Although certain criticisms have been advanced of this form of treatment, there is no doubt that in the hands of the Rhodesian workers it is producing excellent results. Miracil D is the latest form of treatment to be tried out, but the results are anything but promising, certainly with ordinary dosage. There is some evidence that in large doses, e.g., up to 600 mgm., it may prove effective, but these large doses are so liable to produce nausea and vomiting that it is doubtful whether they will prove practical.

Amœbiasis.—The incidence of amœbiasis varies considerably, but the over-all picture is one of considerable urgency. The bacillary form is well controlled by the sulphonamides, but there is no effective remedy for

amœbic dysentery. The major problem here would appear to be adequate control of the acute phase. Emetine is not the last word. It may control the acute form but it cannot be depended upon to cure it, and there is no known remedy which is satisfactory in the treatment of the chronic form. There would appear to be little doubt that a new approach to the problem is necessary and that some fundamental work is required upon the metabolic processes of the amœba to try and discover some preparation which will prove to be a really effective amœbicide.

Tuberculosis.—In practically every area of East and South Africa tuberculosis constitutes a major problem. The condition is so rife that it has so far proved impossible to inaugurate a systematic attack. Whilst the disease usually assumes an acute form, there is some data accumulating which suggests that the more chronic forms are not as rare as is sometimes suggested. The attack here must clearly be twofold: preventive and curative. The former is predominantly a social problem, but no matter how rapidly the living conditions of the native are improved, there will still be ample scope for curative methods. Streptomycin is an obvious weapon here, but the problem is such a vast one that the financial aspects of streptomycin will, for a long time, prove a brake upon its widespread use. On the other hand, there is obvious scope in East Africa for large-scale clinical trials of this antibiotic. Unfortunately I did not have the opportunity of visiting the excellent dispensary organization for the control of tuberculosis which is being carried out on the slopes of Kilimanjaro.

Leprosy.—At long last adequate steps are being taken to bring this historic disease under control. As an essential preliminary, a survey is being made of the incidence of the disease in the East African colonies, a survey which is revealing the vast extent of the problem. Fortunately, the initial results with the newer anti-leprosy preparations, such as diasone and sulphetrone, are promising. In a chronic disease such as leprosy, it is impossible to assess the true value of a remedy until it has been used in a large number of cases over a long period of time, but even the most cautious and most experienced of workers are optimistic. Neither of these preparations is the final answer to this age-long problem, but the results with sulphetrone suggest that it should not be too long before organized research can produce a really effective remedy.

THE OUTLOOK FOR MEDICAL PRACTICE

In these days, medical practitioners, like many other sections of the community, are seriously considering the possibilities of emigration to various parts of the Commonwealth and Empire. To dogmatize is always dangerous, but the following is an attempt to summarize the prospects as they seemed to one visitor. In East Africa, i.e. Kenya, Uganda and Tanganyika, there is little further scope at the moment in private practice. Even in Nairobi, with its relatively large white population, there is really no room for more

SOME COMMON DISEASES

Malaria.—Disappointingly little information was available concerning the relative values of mepacrine and paludrine in prophylaxis. From a mass of contradictory "clinical impressions", the one definite fact that did appear was that whatever the final conclusion might be concerning these two potent preparations, a tablet of paludrine per week would not be the adequate prophylactic dose that it so dramatically proved to be in New Guinea. But what is clearly necessary is a large-scale, carefully controlled investigation of the effect of both these preparations. Of the relative non-toxicity of paludrine, there appeared to be little doubt. One interprising medical officer, for instance, had taken up to ten tablets in one day with impunity! From the curative point of view, the general consensus of opinion was that quinine should be given for the first twenty-four hours, as it controlled the condition more rapidly than any other drug, and that subsequently mepacrine should be given. In the case of adult natives, there were some who believed that, unless it was a severe infection, it was unwise to treat the condition too energetically with any of the antimalarial preparations, as there was some risk in so doing of interfering with the acquired immunity of the patient.

Sleeping sickness.—There is still no effective remedy for the control of infections with *T. rhodesiense*. Cases due to *T. gambiense* respond fairly well to antrypol or suramin if given early enough, but these preparations are of doubtful efficacy in cases due to *T. rhodesiense*. Opinions differed as to the value of tryparsamide. In some areas its use had practically been given up because of its toxicity. There appeared to be considerable difference of opinion as to whether the blindness, which is so liable to develop in these cases, was due to the disease or to the tryparsamide. A certain amount of interest was being evinced in the possible prophylactic value of pentamidine.

Schistosomiasis.—This constitutes one of the major medical problems in Africa, particularly in Egypt, Southern Rhodesia and South Africa. Its gradual spread throughout South Africa is one of the noteworthy features of recent years. From the therapeutic angle, some excellent work is being done in Southern Rhodesia, the home of the intensive antimonial treatment of the disease. Although certain criticisms have been advanced of this form of treatment, there is no doubt that in the hands of the Rhodesian workers it is producing excellent results. Miracil D is the latest form of treatment to be tried out, but the results are anything but promising, certainly with ordinary dosage. There is some evidence that in large doses, e.g., up to 600 mgm., it may prove effective, but these large doses are so liable to produce nausea and vomiting that it is doubtful whether they will prove practical.

Amœbiasis.—The incidence of amœbiasis varies considerably, but the over-all picture is one of considerable urgency. The bacillary form is well controlled by the sulphonamides, but there is no effective remedy for

CURRENT THERAPEUTICS

IX.—ŒSTROGENS

By P. M. F. BISHOP, D.M.

Endocrinologist, Guy's Hospital, and Chelsea Hospital for Women.

IN 1917 Stöckard and Papanicolaou described the vaginal cycle in the guinea-pig. In 1923 Allen and Doisy applied the vaginal smear technique to the mouse and thus elaborated a sensitive test of œstrogenic activity which certainly hastened the isolation of œstrone in 1929 by Doisy, Veler and Thayer, in the United States, and by Butenandt in Germany. In the following year Marrian (1930) isolated œstriol, and in 1933 Schwenk and Hildebrandt prepared œstradiol from œstrone. These discoveries laid the foundations of modern œstrogen therapy; before this time only aqueous extracts of animal ovaries were available, the potency of which was practically negligible. It soon became possible to employ the pure crystalline hormone in high concentration in oil, and standardized in international units, and in 1933 Kaufmann reported the induction of true menstrual bleeding in a castrate following administration of œstradiol benzoate and progesterone. During the next five years the naturally occurring œstrogens were used with increasing enthusiasm for menstrual disorders and menopausal disturbances, the only practical limit to their administration being the unavoidable costliness of the preparations. In 1938 this difficulty was overcome by Dodds and his associates, who introduced a synthetic œstrogen of high oral potency, which was cheap and unprotected by patent. This compound, stilbœstrol, was submitted to clinical trial in this country (Bishop, Boycott and Zuckerman, 1939; Kellar and Sutherland, 1939; Winterton and MacGregor, 1939) and was found to possess all the properties of the naturally occurring œstrogens, although in certain circumstances it induced "toxic" effects, chiefly nausea and occasionally vomiting. Reports of its use soon appeared in the American (Shorr, Robinson and Papanicolaou, 1939) and French literature (Varangot, 1939) in which undue stress was laid on the "toxicity". Shortly after this two other synthetic compounds, hexœstrol and dienœstrol, belonging to the stilbene group, were prepared by Dodds and his colleagues (Dodds, Lawson and Noble, 1938) and made available for clinical use. By that time, however, the outbreak of war made it impossible to submit these preparations to a thorough clinical test, although a report on hexœstrol was made to the Therapeutic Trials Committee (Bishop, *et al.*, 1940). Animal assays had suggested that these compounds might prove even more potent than stilbœstrol itself, and they were consequently employed in considerably smaller doses, at which level "toxic" effects occurred less frequently. It was not until after the war that these œstrogens received a careful clinical

doctors at the moment. Many practitioners have settled there since the end of the war, and until the white population has increased considerably there is practically no scope for the ambitious man. On the other hand, there are excellent prospects in the Colonial Medical Service. At the moment, conditions of service and pay are not satisfactory, but now that the National Health Service has been instituted in Great Britain, there can be no doubt that conditions in the Colonial Medical Service must be brought up to this standard. One word of warning must, however, be interpolated. It is impossible to become proficient in tropical medicine without a sound knowledge of the native and of his mode of living. This knowledge cannot be acquired by living and working in the larger centres such as Nairobi, Kampala and Dar-es-Salaam. The new recruit, for his own sake as well as for the efficient working of the Service, must be prepared to spend his first few years "up country". Too often, of recent years, new entrants to the Service have protested against this procedure, especially if they were married men. It has even been suggested that this reluctance to go on *safari* has been due to lack of the pioneer spirit in the rising generation. One hopes that this accusation is entirely unjustified, but what the new entrant must remember is that no one will benefit more from this arrangement than he himself.

Southern Rhodesia is a country which appeals particularly to the Englishman, but here again the medical profession is tending to be overcrowded, and any practitioner who is thinking of settling in this delightful country should inquire carefully into local conditions before he finally decides to emigrate.

The same remarks apply, but even more forcibly, to the Union of South Africa. The three medical schools in the Union are producing 250 to 300 new graduates every year, and it has been estimated that if the present annual rate of increase of practitioners persists, "it will not be long before doctors in South Africa will be forced to emigrate if they are to continue the practice of medicine" (*Lancet*, 1948, June 5, 886). In the view of the Medical Association of South Africa, whilst "normally an overseas medical man wishing to settle in the Union is welcomed . . . no man would be wise who would give up what he has, to settle here, until at least he had visited the Union—on holiday perhaps—to see things for himself and to make up his mind as to his chances".

physical changes may appear which are due to relative lack of œstrogen, secretion probably does not cease completely.

Superimposed upon this constant basal secretion of œstrogen, which may come from the interstitial cells of the ovary and from the adrenal cortex, there is the secretion of œstradiol from Graafian follicles and active corpora lutea during the years of female maturity. This highly active œstrogen tends to undergo degradation to less active forms such as œstrone and œstriol, or to be conjugated in the liver with glycuronic acid, which renders it less potent. The inactivation of œstrogen is facilitated by progesterone, so that during the post-ovular phase of the ovarian cycle, œstrogen, although it may continue to be secreted by the corpus luteum, perhaps even in higher concentration than during the follicular phase of the cycle, is considerably less effective. Thus, in the woman with normal ovular cycles there is a rhythmic intensification of œstrogenic influences during the first half of her menstrual cycle, alternating with a phase of œstrogenic ineffectiveness during the post-ovular phase. Failure to ovulate or defective progesterone secretion results in constant circulation of œstrogen in a highly active form, and may give rise to functional menstrual disorders such as amenorrhœa or metropathic flooding, or to increase in weight associated with fluid retention.

Yet again, superimposed upon this rhythmical effect of œstrogen and œstrogen-plus-progesterone are the conditions of œstrogen secretion during pregnancy. Here an entirely new gland, the placenta, largely takes over from the ovary the responsibility for producing œstrogen, and secretes it in rapidly increasing and finally very high concentrations. The uterus enlarges, the breasts become swollen, the vagina hypertrophies, the nipples and linea alba become pigmented. Despite these obvious signs of intense œstrogenic stimulation, however, there is also evidence of œstrogenic inactivation. Œstrogens circulate during pregnancy largely in a conjugated form, and as such they are incapable of sensitizing the uterine muscle to respond to the oxytocic effect of posterior pituitary hormone. It is only immediately before parturition that there are found to be circulating in the blood "free" œstrogens which induce the contractions of the uterine muscle to which the onset of labour is due.

An entirely different aspect of œstrogen secretion concerns its relationship to the pituitary, the anterior lobe of which secretes trophic hormones which control the activities of the gonads, the thyroid and the adrenal cortex. Each of these trophic hormones, however, is held in check by the hormones of the glands which they stimulate. Thus, increasing secretion of œstrogen leads to pituitary inhibition, especially in regard to the discharge of gonadotrophic hormones.

ROUTES OF ADMINISTRATION

Œstrogens, particularly stilbœstrol and dienœstrol, are so active *by mouth*

assessment (Bishop, Kennedy and Wynn-Williams, 1948), as the result of which it appears that stilbæstrol is the most potent æstrogen yet available, whereas dienæstrol is three to five times less potent, and hexæstrol about fifteen times less potent. Studies of "toxicity" have shown that for stilbæstrol this depends entirely upon dosage. Dienæstrol and hexæstrol, however, appear to be specifically less "toxic".

ÆSTROGENS AVAILABLE FOR CLINICAL USE

At the present time only five compounds are commonly employed in this country. They are:—

(A) *Natural æstrogens*

Æstrone

Æstradiol benzoate

(B) *Synthetic æstrogens*

Stilbæstrol

Dienæstrol

Hexæstrol

There are, however, a number of other preparations of varying æstrogenic activity which have been marketed either in this country, on the Continent or in the United States and Canada. These include:—

(A) *Natural æstrogens*

Æstriol—said to have considerable oral potency.

Æstrone sulphate—a conjugated æstrogen derived from urine of pregnant mares with a potency of the same order as dienæstrol.

Æstradiol dipropionate—said to give a more prolonged effect than æstradiol benzoate.

(B) *Synthetic æstrogens*

Dibromethylene—D.B.E.—said to have a prolonged oral effect.

Ethinyl æstradiol—commonly used in America, and said to be a highly potent oral æstrogen.

Doisynolic acid—used in Switzerland, and said to be non-toxic and highly potent. It has a range of activity roughly equal to that of dienæstrol.

Some of these compounds, such as æstriol, æstradiol dipropionate, and dibromethylene, have enjoyed a limited and transient popularity in this country. Others, such as æstrone sulphate and ethinyl æstradiol, are likely to attract further attention here in the near future.

THE PHYSIOLOGY OF ÆSTROGENS

The rationale of æstrogen therapy is based upon certain physiological considerations. In the first place æstrogen is secreted constantly both in the male and female organism. This basal secretion may produce minimal æstrogenic effects, as it does in the male, and in the female before the menarche. In the mature female, the effects are obvious, for the constant basal secretion is responsible for the maintenance of such secondary sex characters as the shape of the female breasts, the size of the adult uterus and adnexa, and the "œstrous" condition of the vaginal mucosa. After the menopause, the basal level gradually falls, but although symptoms and

physical changes may appear which are due to relative lack of œstrogen, secretion probably does not cease completely.

Superimposed upon this constant basal secretion of œstrogen, which may come from the interstitial cells of the ovary and from the adrenal cortex, there is the secretion of œstradiol from Graafian follicles and active corpora lutea during the years of female maturity. This highly active œstrogen tends to undergo degradation to less active forms such as œstrone and œstriol, or to be conjugated in the liver with glycuronic acid, which renders it less potent. The inactivation of œstrogen is facilitated by progesterone, so that during the post-ovular phase of the ovarian cycle, œstrogen, although it may continue to be secreted by the corpus luteum, perhaps even in higher concentration than during the follicular phase of the cycle, is considerably less effective. Thus, in the woman with normal ovular cycles there is a rhythmic intensification of œstrogenic influences during the first half of her menstrual cycle, alternating with a phase of œstrogenic ineffectiveness during the post-ovular phase. Failure to ovulate or defective progesterone secretion results in constant circulation of œstrogen in a highly active form, and may give rise to functional menstrual disorders such as amenorrhœa or metropathic flooding, or to increase in weight associated with fluid retention.

Yet again, superimposed upon this rhythmical effect of œstrogen and œstrogen-plus-progesterone are the conditions of œstrogen secretion during pregnancy. Here an entirely new gland, the placenta, largely takes over from the ovary the responsibility for producing œstrogen, and secretes it in rapidly increasing and finally very high concentrations. The uterus enlarges, the breasts become swollen, the vagina hypertrophies, the nipples and linea alba become pigmented. Despite these obvious signs of intense œstrogenic stimulation, however, there is also evidence of œstrogenic inactivation. Œstrogens circulate during pregnancy largely in a conjugated form, and as such they are incapable of sensitizing the uterine muscle to respond to the oxytocic effect of posterior pituitary hormone. It is only immediately before parturition that there are found to be circulating in the blood "free" œstrogens which induce the contractions of the uterine muscle to which the onset of labour is due.

An entirely different aspect of œstrogen secretion concerns its relationship to the pituitary, the anterior lobe of which secretes trophic hormones which control the activities of the gonads, the thyroid and the adrenal cortex. Each of these trophic hormones, however, is held in check by the hormones of the glands which they stimulate. Thus, increasing secretion of œstrogen leads to pituitary inhibition, especially in regard to the discharge of gonadotrophic hormones.

ROUTES OF ADMINISTRATION

Œstrogens, particularly stilbœstrol and dienœstrol, are so active *by mouth*

assessment (Bishop, Kennedy and Wynn-Williams, 1948), as the result of which it appears that stilbæstrol is the most potent æstrogen yet available, whereas dienæstrol is three to five times less potent, and hexæstrol about fifteen times less potent. Studies of "toxicity" have shown that for stilbæstrol this depends entirely upon dosage. Dienæstrol and hexæstrol, however, appear to be specifically less "toxic".

ÆSTROGENS AVAILABLE FOR CLINICAL USE

At the present time only five compounds are commonly employed in this country. They are:—

(A) *Natural æstrogens*

Æstrone

Æstradiol benzoate

(B) *Synthetic æstrogens*

Stilbæstrol

Dienæstrol

Hexæstrol

There are, however, a number of other preparations of varying æstrogenic activity which have been marketed either in this country, on the Continent or in the United States and Canada. These include:—

(A) *Natural æstrogens*

Æstriol—said to have considerable oral potency.

Æstrone sulphate—a conjugated æstrogen derived from urine of pregnant mares with a potency of the same order as dienæstrol.

Æstradiol dipropionate—said to give a more prolonged effect than æstradiol benzoate.

(B) *Synthetic æstrogens*

Dibromethylene—D.B.E.—said to have a prolonged oral effect.

Ethinyl æstradiol—commonly used in America, and said to be a highly potent oral æstrogen.

Doisylic acid—used in Switzerland, and said to be non-toxic and highly potent. It has a range of activity roughly equal to that of dienæstrol.

Some of these compounds, such as æstriol, æstradiol dipropionate, and dibromethylene, have enjoyed a limited and transient popularity in this country. Others, such as æstrone sulphate and ethinyl æstradiol, are likely to attract further attention here in the near future.

THE PHYSIOLOGY OF ÆSTROGENS

The rationale of æstrogen therapy is based upon certain physiological considerations. In the first place æstrogen is secreted constantly both in the male and female organism. This basal secretion may produce minimal æstrogenic effects, as it does in the male, and in the female before the menarche. In the mature female, the effects are obvious, for the constant basal secretion is responsible for the maintenance of such secondary sex characters as the shape of the female breasts, the size of the adult uterus and adnexa, and the "æstrous" condition of the vaginal mucosa. After the menopause, the basal level gradually falls, but although symptoms and

physical changes may appear which are due to relative lack of œstrogen, secretion probably does not cease completely.

Superimposed upon this constant basal secretion of œstrogen, which may come from the interstitial cells of the ovary and from the adrenal cortex, there is the secretion of œstradiol from Graafian follicles and active corpora lutea during the years of female maturity. This highly active œstrogen tends to undergo degradation to less active forms such as œstrone and œstriol, or to be conjugated in the liver with glycuronic acid, which renders it less potent. The inactivation of œstrogen is facilitated by progesterone, so that during the post-ovular phase of the ovarian cycle, œstrogen, although it may continue to be secreted by the corpus luteum, perhaps even in higher concentration than during the follicular phase of the cycle, is considerably less effective. Thus, in the woman with normal ovular cycles there is a rhythmic intensification of œstrogenic influences during the first half of her menstrual cycle, alternating with a phase of œstrogenic ineffectiveness during the post-ovular phase. Failure to ovulate or defective progesterone secretion results in constant circulation of œstrogen in a highly active form, and may give rise to functional menstrual disorders such as amenorrhœa or metropathic flooding, or to increase in weight associated with fluid retention.

Yet again, superimposed upon this rhythmical effect of œstrogen and œstrogen-plus-progesterone are the conditions of œstrogen secretion during pregnancy. Here an entirely new gland, the placenta, largely takes over from the ovary the responsibility for producing œstrogen, and secretes it in rapidly increasing and finally very high concentrations. The uterus enlarges, the breasts become swollen, the vagina hypertrophies, the nipples and linea alba become pigmented. Despite these obvious signs of intense œstrogenic stimulation, however, there is also evidence of œstrogenic inactivation. Œstrogens circulate during pregnancy largely in a conjugated form, and as such they are incapable of sensitizing the uterine muscle to respond to the oxytocic effect of posterior pituitary hormone. It is only immediately before parturition that there are found to be circulating in the blood "free" œstrogens which induce the contractions of the uterine muscle to which the onset of labour is due.

An entirely different aspect of œstrogen secretion concerns its relationship to the pituitary, the anterior lobe of which secretes trophic hormones which control the activities of the gonads, the thyroid and the adrenal cortex. Each of these trophic hormones, however, is held in check by the hormones of the glands which they stimulate. Thus, increasing secretion of œstrogen leads to pituitary inhibition, especially in regard to the discharge of gonadotrophic hormones.

ROUTES OF ADMINISTRATION

Œstrogens, particularly stilbœstrol and dienœstrol, are so active *by mouth*

assessment (Bishop, Kennedy and Wynn-Williams, 1948), as the result of which it appears that stilbæstrol is the most potent æstrogen yet available, whereas dienæstrol is three to five times less potent, and hexæstrol about fifteen times less potent. Studies of "toxicity" have shown that for stilbæstrol this depends entirely upon dosage. Dienæstrol and hexæstrol, however, appear to be specifically less "toxic".

ÆSTROGENS AVAILABLE FOR CLINICAL USE

At the present time only five compounds are commonly employed in this country. They are:—

(A) *Natural æstrogens*

Æstrone

Æstradiol benzoate

(B) *Synthetic æstrogens*

Stilbæstrol

Dienæstrol

Hexæstrol

There are, however, a number of other preparations of varying æstrogenic activity which have been marketed either in this country, on the Continent or in the United States and Canada. These include:—

(A) *Natural æstrogens*

Æstriol—said to have considerable oral potency.

Æstrone sulphate—a conjugated æstrogen derived from urine of pregnant mares with a potency of the same order as dienæstrol.

Æstradiol dipropionate—said to give a more prolonged effect than æstradiol benzoate.

(B) *Synthetic æstrogens*

Dibromethylene—D.B.E.—said to have a prolonged oral effect.

Ethinyl æstradiol—commonly used in America, and said to be a highly potent oral æstrogen.

Doisynolic acid—used in Switzerland, and said to be non-toxic and highly potent.

It has a range of activity roughly equal to that of dienæstrol.

Some of these compounds, such as æstriol, æstradiol dipropionate, and dibromethylene, have enjoyed a limited and transient popularity in this country. Others, such as æstrone sulphate and ethinyl æstradiol, are likely to attract further attention here in the near future.

THE PHYSIOLOGY OF ÆSTROGENS

The rationale of æstrogen therapy is based upon certain physiological considerations. In the first place æstrogen is secreted constantly both in the male and female organism. This basal secretion may produce minimal æstrogenic effects, as it does in the male, and in the female before the menarche. In the mature female, the effects are obvious, for the constant basal secretion is responsible for the maintenance of such secondary sex characters as the shape of the female breasts, the size of the adult uterus and adnexa, and the "æstrous" condition of the vaginal mucosa. After the menopause, the basal level gradually falls, but although symptoms and

physical changes may appear which are due to relative lack of œstrogen, secretion probably does not cease completely.

Superimposed upon this constant basal secretion of œstrogen, which may come from the interstitial cells of the ovary and from the adrenal cortex, there is the secretion of œstradiol from Graafian follicles and active corpora lutea during the years of female maturity. This highly active œstrogen tends to undergo degradation to less active forms such as œstrone and œstriol, or to be conjugated in the liver with glycuronic acid, which renders it less potent. The inactivation of œstrogen is facilitated by progesterone, so that during the post-ovular phase of the ovarian cycle, œstrogen, although it may continue to be secreted by the corpus luteum, perhaps even in higher concentration than during the follicular phase of the cycle, is considerably less effective. Thus, in the woman with normal ovular cycles there is a rhythmic intensification of œstrogenic influences during the first half of her menstrual cycle, alternating with a phase of œstrogenic ineffectiveness during the post-ovular phase. Failure to ovulate or defective progesterone secretion results in constant circulation of œstrogen in a highly active form, and may give rise to functional menstrual disorders such as amenorrhœa or metropathic flooding, or to increase in weight associated with fluid retention.

Yet again, superimposed upon this rhythmical effect of œstrogen and œstrogen-plus-progesterone are the conditions of œstrogen secretion during pregnancy. Here an entirely new gland, the placenta, largely takes over from the ovary the responsibility for producing œstrogen, and secretes it in rapidly increasing and finally very high concentrations. The uterus enlarges, the breasts become swollen, the vagina hypertrophies, the nipples and linea alba become pigmented. Despite these obvious signs of intense œstrogenic stimulation, however, there is also evidence of œstrogenic inactivation. Œstrogens circulate during pregnancy largely in a conjugated form, and as such they are incapable of sensitizing the uterine muscle to respond to the oxytocic effect of posterior pituitary hormone. It is only immediately before parturition that there are found to be circulating in the blood "free" œstrogens which induce the contractions of the uterine muscle to which the onset of labour is due.

An entirely different aspect of œstrogen secretion concerns its relationship to the pituitary, the anterior lobe of which secretes trophic hormones which control the activities of the gonads, the thyroid and the adrenal cortex. Each of these trophic hormones, however, is held in check by the hormones of the glands which they stimulate. Thus, increasing secretion of œstrogen leads to pituitary inhibition, especially in regard to the discharge of gonadotrophic hormones.

ROUTES OF ADMINISTRATION

Œstrogens, particularly stilbœstrol and dienœstrol, are so active *by mouth*

that there is seldom any need to give them by any other route. In the case of stilbæstrol, however, "toxicity" occasionally limits dosage, although dienæstrol (in two to three times the weight-for-weight dose of stilbæstrol) may be effective without producing nausea. If not, natural æstrogens are indicated. Æstrone, however, is expensive, and less than one-tenth as potent as stilbæstrol. Æstrone sulphate or ethinyl æstradiol, a partially synthesized æstrogen, would no doubt be suitable were they generally available. Therefore on such rare occasions æstradiol benzoate should be given *by injection*. Injection of synthetic æstrogens is never indicated, for they are probably equally effective orally, and injection does not lessen the tendency to "toxic" effects, which are central rather than alimentary in origin.

Other routes of administration have been advocated. From "linguets" placed under the tongue, or between the gum and upper lip, the hormone passes *through the buccal mucosa* directly into the blood stream, leading to more complete absorption. *Inunction* of an æstrogen ointment increases the local effect and has been used in the treatment of poorly developed breasts. Vaginal and rectal *suppositories* are also said to produce local concentration in the neighbourhood of such "target organs" as the vagina in atrophic vaginitis, and the uterus in menstrual disorders. Prolongation of action is claimed for injection of aqueous suspensions of "*micro-crystals*", although *implantation* of crystalline hormone pellets produces a constant effect of considerably greater duration, up to eight or nine months for a 100 mgm. pellet of stilbæstrol, and up to two years for a 100 mgm. pellet of æstradiol.

DOSAGE

It is not perhaps sufficiently recognized how important it is to determine the correct dose of æstrogen for each individual patient, for it is rare to be told, when a patient is referred, what dose of æstrogen has been given: "This patient has been on stilbæstrol" is the usual comment, as though it mattered little whether the dose was 1 mgm. a day for a fortnight or 1 mgm. thrice daily for two years.

In conditions such as *the menopausal syndrome* it is essential to determine the lowest dose which will control the symptoms, for if this dose is grossly exceeded, not only may there be an "escape" from the therapeutic effect, with return of hot flushes, but other manifestations such as distension and headaches may appear, apart from the inconvenience of uterine bleeding. It is unfortunately impossible, however, to fix a standard dose, for whereas as little as 0.1 mgm. daily of stilbæstrol, or even 3000 I.U. of æstrone, may be adequate in some cases, others may require 1 mgm. of stilbæstrol a day, and at this level there is considerable likelihood of bleeding and nausea.

In the treatment of *menstrual disorders* slightly higher doses are needed: 1 to 3 mgm. daily of stilbæstrol for a fortnight will usually induce an "æstrogen withdrawal bleeding" in amenorrhœa, although occasionally

5 mgm. will be required. In a woman with regular ovular cycles, however, more than 2 mgm. of stilbæstrol given daily during the first half of the cycle, for dysmenorrhœa for instance, or to improve the cervical secretion in cases of sterility due to "cervical hostility", may prevent ovulation. On the other hand, when œstrogens are used to stop uterine bleeding, as in a metropathic flooding, the hæmostatic dose is much higher, and 5 mgm. of stilbæstrol should be given four-hourly with a maintenance dose of 5 mgm. daily for a week following the cessation of bleeding.

In pregnancy and immediately post-partum high doses are required and are always well tolerated. For instance, at least 15 mgm. should be given for the first few days to inhibit or suppress lactation, with a maintenance dose of 10 mgm. daily for another week or ten days.

On occasion, short intensive courses are justified, for example to relieve an intractable kraurosis or senile vaginitis, but they should be given deliberately and after due consideration of the possibility of such complications as a brisk uterine hæmorrhage.

When œstrogens are employed for their inhibitory effect on the pituitary, as in *carcinoma of the prostate*, large doses given constantly must be used, and a daily dose of 15 mgm. of stilbæstrol is required, or better still an implantation of 200 or 300 mgm. The occurrence of gynæcomastia and impotence is to be expected rather than regarded as an undesirable complication.

On the other hand, it must be realized that constant administration of œstrogen in all but minimal doses, such as are used for the menopause, tends to inhibit the pituitary and may lead to permanent functional damage of this gland. It is therefore always undesirable, except at the menopause in minimal doses, or in such conditions as carcinoma of the prostate, to give œstrogens for longer than three weeks at a time, with an interval of at least a week between successive courses.

THERAPEUTIC INDICATIONS

The menopause.—This is a condition of gradually waning ovarian function, of which there are two implications. In the first place it leads to a disturbance of the reciprocal gonadotrophic-œstrogen balance; as the level of œstrogen secreted by the ovary falls, the follicle-stimulating hormone (F.S.H.) secretion increases. Indeed some authorities hold that the menopausal syndrome is due to the increased F.S.H. circulation rather than to the diminished œstrogen output, and advocate the administration of androgens to inhibit the pituitary. It would seem more plausible, however, to regard the lowered œstrogen level as the primary disturbance and to give *small doses* of œstrogen as a therapeutic measure. The second implication of the gradually failing ovarian function is that ovulation ceases to take place and no progesterone is secreted. The organism is therefore under the constant influence of œstrogen although its level of production is considerably

lowered. Nevertheless, this constant œstrogen influence tends to give rise to symptoms of nervous tension, headaches, and abdominal distension, not infrequently experienced by women in the premenstrual week. Administration of unnecessarily large doses of œstrogen aggravates these symptoms, and they may be just as distressing as the true menopausal complaints. The symptoms of the artificially induced menopause are often more severe and prolonged than those of the naturally occurring condition, and are not so easily controlled. This fact should be carefully considered by a gynaecologist in choosing between radium or deep X-ray destruction of the ovary and hysterectomy for the treatment of functional uterine bleeding.

Amenorrhœa.—Administration of œstrogens alone can usually produce "œstrogen withdrawal bleeding" in cases of amenorrhœa. Provided the dose is one which will just produce withdrawal bleeding, there may be some stimulant effect on the ovary, with restoration of normal menstrual rhythm, but this occurs in only a small percentage of cases, and on the whole the results are so disappointing that it is doubtful whether it is worth while trying to treat amenorrhœa *per se*. Certainly prolonged administration of œstrogens, especially in doses of more than 1 mgm. of stilbœstrol daily, should be deprecated, for not only may it inhibit uterine bleeding, or cause troublesome flooding, but it may also lead to permanent damage to the pituitary. Small doses of œstrogen (0.5 mgm. of stilbœstrol daily for twenty-one days, given in combination with 30 mgm. of ethisterone daily during the last seven days of the course) sometimes cause uterine hæmorrhage, and when the treatment is discontinued after three or four courses, two or three spontaneous ovular cycles may result. This treatment is therefore indicated in certain cases of infertility due to failure to ovulate.

Excessive uterine hæmorrhage.—High doses (5 mgm. of stilbœstrol every four hours) can stop uterine flooding in twenty-four to thirty-six hours, and a maintenance dose of 5 mgm. daily for three weeks, with four injections of 10 mgm. of progesterone on alternate days in the next week, will be followed by bleeding which is normal in amount. Repeated courses of the maintenance dose of œstrogen followed by the progesterone may tide over a difficult phase of metropathia. Indeed, it may even be possible to achieve this with the progesterone course alone, repeated every twenty-eight days.

Dysmenorrhœa.—Painless scanty œstrogen withdrawal bleeding can always be induced in cases of true spasmodic dysmenorrhœa if stilbœstrol is given in daily doses of 3 mgm. or more for a fortnight, starting within the first three or four days of the cycle. It may, however, be undesirable to persist in this form of treatment, which can lead to irregular and heavy bleeding. A smaller dose given earlier in the cycle may induce a natural painless period at the expected time, but it is sometimes difficult to find this dose, and not always possible to repeat the effect in subsequent cycles. Sometimes a relatively small dose of œstrogen produces neither a withdrawal bleeding nor a normal painless period, but prolongs the cycle by about a

fortnight. There is no theoretical reason why œstrogens should *cure* dysmenorrhœa, and if it is thought that the condition can be permanently relieved by other procedures, such as dilatation of the cervix, they should be preferred to endocrine therapy.

Estrogens in pregnancy.—œEstrogens may be given in large doses (up to 15 mgm. daily) to stimulate uterine contractions and thus evacuate the uterus in cases of missed abortion or uterine inertia, and, according to Smith and Smith (1942), in similar doses for the treatment of toxæmia or pre-eclampsia. Doses of the same order are effective in suppressing lactation post-partum.

Estrogens and cancer—Prolonged administration of œstrogen increases the incidence of cancer, especially of the breast, in certain strains of mice. It seems doubtful, however, if these findings can be applied to the human subject, although it might be unwise to prolong œstrogen administration in a woman with a strong family history of breast cancer, and it would be neither advisable, nor indeed indicated, to treat chronic mastitis or leukoplakia vulvæ with œstrogens. There is, in fact, some evidence that intensive œstrogen therapy may lead to temporary regression of carcinoma of the breast in post-menopausal women, although in younger women androgens or castration have been advocated. Perhaps the effect in older women is due to the inhibitory action of œstrogens on the pituitary, which, at this age, shows signs of over-activity by secreting excessive amounts of F.S.H. It is at the same age that carcinoma of the prostate develops, and œstrogens certainly lead in a remarkable manner to regression of the prostatic growth and its secondaries, although unfortunately the relief appears to be temporary, for after about five years of treatment the condition resumes its remorseless course.

Other applications of œstrogen therapy.—Apart from the conditions discussed, the principal use of œstrogens is in the field of dermatology. Certain post-climacteric disorders, such as *atrophic vaginitis*, are well-recognized as being due to œstrogen deficiency and usually respond satisfactorily to short intensive courses of treatment. But there are other conditions for which œstrogen has been used, more or less empirically, because they occur almost exclusively in post-menopausal women, or at the time of the menstrual flow, when the effective œstrogen level is known to be low. For instance, *keratoderma* of the palms of the hands and soles of the feet usually appears after the menopause. Although not generally recognized it is probably not an uncommon syndrome and is usually relieved in a month or so by moderate doses of œstrogen. Another condition is the circumscribed *ulcer inside the cheeks* or on the tongue or gums, sometimes associated with similar ulcers on the vulva. At first confined to the period of the menstrual flow, they are later almost continuously present. They are generally relieved by œstrogens, although high doses may have to be maintained for some weeks. Finally, *acne*, or rather the seborrhœic condition of

the skin on which the acne flourishes, is an androgenic manifestation which may be overcome by œstrogen administration, although prolonged courses of rather high dosage may be needed. In the male this is seldom justified because of the danger of testicular atrophy. In adolescent girls, however, relief may be achieved by administration of courses of 3 mgm. of stilbœstrol daily during the first half of the cycle. Unfortunately this anti-androgenic effect of œstrogens is not successful in the case of hirsutism and hypertrichosis.

œstrogen therapy has been advocated for many other conditions, such as atrophic rhinitis and gingivitis, menopausal psychopathic disorders and climacteric arthritis, Cushing's syndrome, and acromegaly, but such treatment is not sufficiently well-established to warrant detailed discussion at present.

References

- Allen, E., and Doisy, E. A. (1923): *J. Amer. med. Ass.*, **81**, 819.
 Bishop, P. M. F., Boycott, M., and Zuckerman, S. (1939): *Lancet*, **i**, 5.
 —, *et al.* (1940): *Ibid.*, **i**, 629.
 —, Kennedy, G. C., and Wynn-Williams, G. (1948): (In the press).
 Butenandt, A. (1929): *Deutsch. med. Wschr.*, **55**, 2177.
 Dodds, E. C., *et al.* (1938): *Nature*, **141**, 247.
 —, Lawson, W., and Noble, R. L. (1938): *Lancet*, **i**, 1389.
 Doisy, E. A., Veler, E. D., and Thayer, S. (1929): *Amer. J. Physiol.*, **90**, 329.
 Kaufman, C. (1933): *Zbl. Gynäk.*, **57**, 42.
 Kellar, R. J., and Sutherland, J. K. (1939): *J. Obstet. Gynec. Brit. Emp.*, **46**, 1.
 Marrian, G. F. (1930): *Biochem. J.*, **24**, 1021.
 Schwenck, E., and Hildebrandt, F. (1933): *Naturwissenschaften*, **21**, 177.
 Shorr, E., Robinson, F. H., and Papanicolaou, G. N. (1939): *J. Amer. med. Ass.*, **113**, 2312.
 Smith, G. V., and Smith, O. W. (1942): *J. clin. Endocrinol.*, **1**, 477.
 Stockard, C. N., and Papanicolaou, G. N. (1917): *Amer. J. Anat.*, **22**, 225.
 Varangot, J. (1939): *Presse méd.*, **38**, 725.
 Winterton, W. R., and MacGregor, T. N. (1939): *Brit. med. J.*, **i**, 10.

REVISION CORNER

THE CHOICE OF SULPHONAMIDES

A NOTE on this subject was published in *The Practitioner*, in January 1946 (vol. 156, p. 72). Since then there have been no fundamental changes, but a few modifications in emphasis have become desirable through greater experience, improved supplies, and the wider availability of penicillin. Before considering these, the opportunity must be taken to urge that sulphonamides should be prescribed or ordered only by the official or semi-official names, e.g., those used in the M.R.C. War Memorandum No. 10 on "The Medical Use of Sulphonamides". It is these names which are used in this article. The use of trade names is liable to cause confusion and to render supply difficult.

The choice of which sulphonamide to use in any particular case depends upon several different principles:—

(1) *Degree of activity against bacteria*, usually measured *in vitro*.—For all practical purposes the difference between the sulphonamides is quantitative rather than qualitative, i.e., some compounds are more active than others, but there is no specificity so that one organism, e.g. staphylococcus, is sensitive to one compound whilst another organism is sensitive to an entirely different compound. The advantage of using certain compounds for certain infections depends rather upon the different distribution of the compounds in the body, e.g. sulphathiazole, which is excreted rapidly in the urine, is especially useful for the treatment of urinary infections. As measured in the test tube, sulphathiazole is probably the most active compound; sulphadiazine, sulphamezathine (sulphadimethylpyrimidine), and sulphapyridine are almost as active; sulphanilamide, sulphacetamide and similar compounds are much less active, particularly against pneumococcal infections.

(2) *Height and duration of blood concentration reached with therapeutic doses*.—Sulphamerazine, sulphamezathine, and sulphadiazine (in this order) are advantageous in that persistently high blood concentrations can be produced by relatively small, infrequent doses. With sulphathiazole, on the other hand, it is more difficult to maintain a satisfactory level in the blood owing to its rapid excretion.

(3) *Distribution in the body*.—Sulphaguanidine, succinyl sulphathiazole and phthalyl sulphathiazole persist in the lumen of the intestine longer than the others, and so are especially effective against dysentery. Sulphathiazole, as already pointed out, is excreted rapidly in the urine and is therefore useful in urinary infections.

(4) *Tendency to produce toxic reactions*.—Sulphadimethylpyrimidine and sulphanilamide are probably the least toxic. Sulphadiazine also causes few toxic reactions, but occasionally it causes obstruction in the urinary passages, if the patient is not well supplied with fluids. Sulphathiazole is more apt than the others to produce sensitization, e.g. drug fever, rash. Sulphapyridine is prone to cause vomiting and should be discarded from clinical use on this account.

(5) *Sensitization*.—If a sulphonamide has been given in the two previous years, it is well to try a different compound in order to diminish the probability of reactions due to sensitization by the earlier treatment; but such sensitization often extends to other sulphonamides besides the one which initially produced it.

(6) *Expense*.—The prices of the different compounds vary from time to time and up-to-date information on this subject is best obtained from the local pharmacist. A recent inquiry elicited the following prices per 100 tablets:—sulphanilamide 2s. 3d.; sulphapyridine 9s.; sulphathiazole 5s. 9d.; sulphadiazine 17s. 6d.; sulphamerazine 20s. 3d.; sulphamezathine 12s.; sulphacetamide 17s. 6d.; sulphaguanidine 5s. 3d.; succinyl sulphathiazole 31s. 6d.; phthalyl sulphathiazole 13s. 6d. According

the skin on which the acne flourishes, is an androgenic manifestation which may be overcome by œstrogen administration, although prolonged courses of rather high dosage may be needed. In the male this is seldom justified because of the danger of testicular atrophy. In adolescent girls, however, relief may be achieved by administration of courses of 3 mgm. of stilbœstrol daily during the first half of the cycle. Unfortunately this anti-androgenic effect of œstrogens is not successful in the case of hirsutism and hypertrichosis.

œstrogen therapy has been advocated for many other conditions, such as atrophic rhinitis and gingivitis, menopausal psychopathic disorders and climacteric arthritis, Cushing's syndrome, and acromegaly, but such treatment is not sufficiently well-established to warrant detailed discussion at present.

References

- Allen, E., and Doisy, E. A. (1923): *J. Amer. med. Ass.*, **81**, 819.
 Bishop, P. M. F., Boycott, M., and Zuckerman, S. (1939): *Lancet*, **i**, 5.
 —, et al. (1940): *Ibid.*, **i**, 629.
 —, Kennedy, G. C., and Wynn-Williams, G. (1948): (In the press).
 Butenandt, A. (1929): *Deutsch. med. Wschr.*, **55**, 2177.
 Dodds, E. C., et al. (1938): *Nature*, **141**, 247.
 —, Lawson, W., and Noble, R. L. (1938): *Lancet*, **i**, 1389.
 Doisy, E. A., Veler, E. D., and Thayer, S. (1929): *Amer. J. Physiol.*, **90**, 329.
 Kaufman, C. (1933): *Zbl. Gynäk.*, **57**, 42.
 Kellar, R. J., and Sutherland, J. K. (1939): *J. Obstet. Gynec. Brit. Emp.*, **46**, 1.
 Marrian, G. F. (1930): *Biochem. J.*, **24**, 1021.
 Schwenck, E., and Hildebrandt, F. (1933): *Naturwissenschaften*, **21**, 177.
 Shorr, E., Robinson, F. H., and Papanicolaou, G. N. (1939): *J. Amer. med. Ass.*, **113**, 2312.
 Smith, G. V., and Smith, O. W. (1942): *J. clin. Endocrinol.*, **1**, 477.
 Stockard, C. N., and Papanicolaou, G. N. (1917): *Amer. J. Anat.*, **22**, 225.
 Varangot, J. (1939): *Presse méd.*, **38**, 725.
 Winterton, W. R., and MacGregor, T. N. (1939): *Brit. med. J.*, **i**, 10.

REVISION CORNER

THE CHOICE OF SULPHONAMIDES

A NOTE on this subject was published in *The Practitioner*, in January 1946 (vol. 156, p. 72). Since then there have been no fundamental changes, but a few modifications in emphasis have become desirable through greater experience, improved supplies, and the wider availability of penicillin. Before considering these, the opportunity must be taken to urge that sulphonamides should be prescribed or ordered only by the official or semi-official names, e.g., those used in the M.R.C. War Memorandum No. 10 on "The Medical Use of Sulphonamides". It is these names which are used in this article. The use of trade names is liable to cause confusion and to render supply difficult.

The choice of which sulphonamide to use in any particular case depends upon several different principles:—

(1) *Degree of activity against bacteria*, usually measured *in vitro*.—For all practical purposes the difference between the sulphonamides is quantitative rather than qualitative, i.e., some compounds are more active than others, but there is no specificity so that one organism, e.g. staphylococcus, is sensitive to one compound whilst another organism is sensitive to an entirely different compound. The advantage of using certain compounds for certain infections depends rather upon the different distribution of the compounds in the body, e.g. sulphathiazole, which is excreted rapidly in the urine, is especially useful for the treatment of urinary infections. As measured in the test tube, sulphathiazole is probably the most active compound; sulphadiazine, sulphamezathine (sulphadimethylpyrimidine), and sulphapyridine are almost as active; sulphanilamide, sulphacetamide and similar compounds are much less active, particularly against pneumococcal infections.

(2) *Height and duration of blood concentration reached with therapeutic doses*.—Sulphamerazine, sulphamezathine, and sulphadiazine (in this order) are advantageous in that persistently high blood concentrations can be produced by relatively small, infrequent doses. With sulphathiazole, on the other hand, it is more difficult to maintain a satisfactory level in the blood owing to its rapid excretion.

(3) *Distribution in the body*.—Sulphaguanidine, succinyl sulphathiazole and phthalyl sulphathiazole persist in the lumen of the intestine longer than the others, and so are especially effective against dysentery. Sulphathiazole, as already pointed out, is excreted rapidly in the urine and is therefore useful in urinary infections.

(4) *Tendency to produce toxic reactions*.—Sulphadimethylpyrimidine and sulphanilamide are probably the least toxic. Sulphadiazine also causes few toxic reactions, but occasionally it causes obstruction in the urinary passages, if the patient is not well supplied with fluids. Sulphathiazole is more apt than the others to produce sensitization, e.g. drug fever, rash. Sulphapyridine is prone to cause vomiting and should be discarded from clinical use on this account.

(5) *Sensitization*.—If a sulphonamide has been given in the two previous years, it is well to try a different compound in order to diminish the probability of reactions due to sensitization by the earlier treatment; but such sensitization often extends to other sulphonamides besides the one which initially produced it.

(6) *Expense*.—The prices of the different compounds vary from time to time and up-to-date information on this subject is best obtained from the local pharmacist. A recent inquiry elicited the following prices per 100 tablets:—sulphanilamide 2s. 3d.; sulphapyridine 9s.; sulphathiazole 5s. 9d.; sulphadiazine 17s. 6d.; sulphamerazine 20s. 3d.; sulphamezathine 12s.; sulphacetamide 17s. 6d.; sulphaguanidine 5s. 3d.; succinyl sulphathiazole 31s. 6d.; phthalyl sulphathiazole 13s. 6d. According

to this price list, the best value for the least expense is obtained from sulphanilamide, sulphathiazole, sulphamezathine, sulphaguanidine, and phthalyl sulphathiazole. The prices of these compounds when supplied under trade or brand names are often much higher.

(7) *Supply*.—This was often the deciding factor in war time, but it should no longer require consideration.

INDIVIDUAL SULPHONAMIDES

The chief features of the sulphonamides in common use are as follows:—

Sulphanilamide is cheap, fairly well tolerated and comparatively soluble. It is not very potent, however, and its use should be restricted to moderately severe infections by hæmolytic streptococci and to local application to the peritoneum or to wounds; it may also be used as a base for the local application of penicillin.

TABLE SHOWING WHICH SULPHONAMIDE TO USE IN DIFFERENT CONDITIONS

Condition	Sulphonamide (in order of preference)
Hæmolytic streptococcal infections Otitis media Pneumonia Chancroid Lymphogranuloma inguinale Gonorrhœa (if penicillin is not available)	Sulphamezathine, sulphadiazine, sulphathiazole
Meningitis	Sulphadiazine, sulphamezathine, sulphathiazole
Urinary infections	Sulphathiazole, sulphamezathine
Wounds and burns (local application, if penicillin is not available)	Sulphathiazole, or a mixture of this and sulphanilamide
Peritonitis (local application)	Sulphathiazole, sulphamezathine, sulphadiazine
Bacillary dysentery	Phthalyl sulphathiazole, sulphaguanidine, sulphadiazine (or sulphamezathine)
Prophylaxis against rheumatic fever or meningococcal or streptococcal infections	Sulphamerazine, sulphamezathine, sulphadiazine

Sulphapyridine is effective but toxic and its use is not recommended.

Sulphathiazole is highly active, and not very toxic apart from its tendency to produce sensitization; it may occasionally cause obstruction in the urinary passages. It is rapidly excreted, however, and large and frequent doses are required to maintain a satisfactory blood concentration. It is a satisfactory compound for general purposes but sulphamezathine is better. Although the best sulphonamide for the local application to the peritoneum or to wounds, it has been overshadowed or supplanted by penicillin.

Sulphadiazine is highly active and in a moderate dosage produces a high and persistent blood concentration. Although it may occasionally block the urinary passages, it is relatively non-toxic. It diffuses into the cerebrospinal fluid better than sulphamezathine. It is good for insertion into the peritoneum.

Sulphamezathine (sulphadimethylpyrimidine) is similar to sulphadiazine but is more soluble and does not block the urinary passages. It also produces higher

blood concentrations. It is probably the best sulphonamide for general use.

Sulphamerazine (sulphamethylpyrimidine) also resembles sulphadiazine but excretion is slow, so that the same blood concentration can be maintained with lower and less frequent dosage than is necessary with sulphadiazine. Accordingly it is particularly useful for prophylaxis.

Sulphaguanidine tends to remain in the intestine to a greater extent than the above compounds but its antibacterial activity is only moderate. Its use should be limited to moderately severe cases of bacillary dysentery.

Phthalyl sulphathiazole is not absorbed to any significant extent, but it breaks down in the intestine to liberate small amounts of sulphathiazole. It is most effective in suppressing coliform bacilli in the intestine and it is non-toxic. Its use is restricted to bacillary dysentery and to the preoperative preparation of patients before surgical operation on the colon. Succinyl sulphathiazole is similar but is slightly less active.

Thus out of the score or more of sulphonamide compounds which are readily available a small group may be selected for regular use, i.e. sulphamezathine for most general purposes, sulphamerazine for prophylaxis, and phthalyl sulphathiazole for bacillary dysentery and preoperative preparation of the colon. Sulphadiazine and sulphathiazole may be used instead of sulphamezathine as shown in the table. It is often an advantage to use three sulphonamides in combination as their total solubility is thereby increased and there is less danger of blocking the urinary passages. Any three out of the four—sulphamezathine, sulphadiazine, sulphamerazine and sulphathiazole—are suitable.

F. HAWKING, D.M.

THE TREATMENT OF HEADACHE

THE fact that headache is only a symptom and that its treatment is the treatment of the pathological process causing it cannot be overstressed. Only too often this obvious and elementary therapeutic principle tends to be lost sight of, and symptomatic remedies are prescribed when only a careful and accurate assessment of the underlying disease holds any prospect of relieving the patient's suffering.

PSYCHIATRY

In the majority of cases the headache will be found to be of psychogenic origin. In the hysterical group, treatment may be one of the most difficult problems in medicine. An explanation of the mode of origin of the headache, together with sedatives and such adjustment of a provocative background as is practicable, may relieve a few, but in many cases it will fail or even aggravate the condition, producing a reaction characterized by the remark that "My doctor does not understand my illness". In such circumstances the patient often seeks the aid of the osteopath, or the dietitian, and it is humiliating but understandable that in such hands they often obtain the relief that we have failed to give them. In those whom the general practitioner and general physician cannot cure and who do not stray from the fold of orthodox medicine the psychiatrist can often be of very real help. In the far larger group due to anxiety, firm reassurance regarding the absence of organic disease together with a careful and tactful explanation as to how the symptoms have arisen, sedatives, and the removal of mental and emotional stress, so far as this is possible, will relieve nearly every case. However, tension headaches usually arise in the psychologically inadequate and their symptoms tend to recur in the same or another guise whenever the easy tenor of their life is disturbed.

MIGRAINE

In migraine it will often be found that the patient is over-conscientious and excessively hard working and has ambitions which are quite beyond the reach of his

to this price list, the best value for the least expense is obtained from sulphanilamide, sulphathiazole, sulphamezathine, sulphaguanidine, and phthalyl sulphathiazole. The prices of these compounds when supplied under trade or brand names are often much higher.

(7) *Supply*.—This was often the deciding factor in war time, but it should no longer require consideration.

INDIVIDUAL SULPHONAMIDES

The chief features of the sulphonamides in common use are as follows:—

Sulphanilamide is cheap, fairly well tolerated and comparatively soluble. It is not very potent, however, and its use should be restricted to moderately severe infections by hæmolytic streptococci and to local application to the peritoneum or to wounds; it may also be used as a base for the local application of penicillin.

TABLE SHOWING WHICH SULPHONAMIDE TO USE IN DIFFERENT CONDITIONS

Condition	Sulphonamide (in order of preference)
Hæmolytic streptococcal infections Otitis media Pneumonia Chancroid Lymphogranuloma inguinale Gonorrhœa (if penicillin is not available)	Sulphamezathine, sulphadiazine, sulphathiazole
Meningitis	Sulphadiazine, sulphamezathine, sulphathiazole
Urinary infections	Sulphathiazole, sulphamezathine
Wounds and burns (local application, if penicillin is not available)	Sulphathiazole, or a mixture of this and sulphanilamide
Peritonitis (local application)	Sulphathiazole, sulphamezathine, sulphadiazine
Bacillary dysentery	Phthalyl sulphathiazole, sulphaguanidine, sulphadiazine (or sulphamezathine)
Prophylaxis against rheumatic fever or meningococcal or streptococcal infections	Sulphamerazine, sulphamezathine, sulphadiazine

Sulphapyridine is effective but toxic and its use is not recommended.

Sulphathiazole is highly active, and not very toxic apart from its tendency to produce sensitization; it may occasionally cause obstruction in the urinary passages. It is rapidly excreted, however, and large and frequent doses are required to maintain a satisfactory blood concentration. It is a satisfactory compound for general purposes but sulphamezathine is better. Although the best sulphonamide for the local application to the peritoneum or to wounds, it has been overshadowed or supplanted by penicillin.

Sulphadiazine is highly active and in a moderate dosage produces a high and persistent blood concentration. Although it may occasionally block the urinary passages, it is relatively non-toxic. It diffuses into the cerebrospinal fluid better than sulphamezathine. It is good for insertion into the peritoneum.

Sulphamezathine (sulphadimethylpyrimidine) is similar to sulphadiazine but is more soluble and does not block the urinary passages. It also produces higher

traction on pain-sensitive structures, treatment depends upon the nature of the lesion. In subdural hæmatoma, abscess and many cases of tumour surgical treatment is indicated. However, in pituitary tumours surgical treatment is better avoided unless vision is threatened, and deep X-irradiation is usually the treatment of choice, whereas in metastatic cerebral tumours surgical treatment should never be considered. The headache of cerebral tumour is usually relieved temporarily by 50 c.cm. of 50 per cent. glucose intravenously, or six ounces of 30 per cent. magnesium sulphate solution per rectum, and in some cases in which removal of the tumour is impossible and headache is intense, palliative decompression may be justifiable.

A. G. W. WHITFIELD, M.B., M.R.C.P.

NOTES AND QUERIES

Fibrous Nodules on the Fingers

QUERY.—About two years ago a schoolgirl noticed that her fingers were a little swollen in the regions of the proximal interphalangeal joints. She came to me about four months ago. I felt one little swelling, of a slightly tense character over one joint, about the size of a small pea. "Ah! a little ganglion" I thought. But then passing along the fingers I found similar protuberances over the dorsal aspects of all the fingers (excepting the thumbs), in the region of the interphalangeal joints. The size varied from that of a very small pea to a fairly large sized one. But not all were of the same consistency: some were more like thickened synovial protuberances, hardly tense at all; others were tenser; and one or two were not uniform but tended to be slightly irregular or nodular. I considered immature Herberden's nodes, gouty deposits, and the ganglion until I saw the symmetrical distribution. Within the past two months the swellings have increased slightly in size. Thinking that they might be gouty I gave a course of cinchophen with no favourable results. Can you help me? I am completely baffled.

REPLY.—The condition is apparently a characteristic example of the fibrous nodules termed in England "knuckle pads", as described by A. E. Garrod, W. Hale White and others. They vary in size from a split pea to a small hazel-nut, and are seldom painful or tender, or troublesome in anyway, except for the slight disfigurement which they cause. They are situated in the deep cutis and subcutaneous tissue over the extensor surface of the proximal interphalangeal joint of one, or usually more fingers (but not the thumbs), are easily movable over the bone but fairly closely attached to the skin, which is naturally somewhat hyperkeratotic over them. They may appear at any age from youth onwards, and are self-limiting, generally reaching their maximum in a few weeks or months. There

may occasionally be a familial history. When once developed they never disappear spontaneously. Small necrobiotic nodules of the rheumatoid arthritic type may sometimes simulate them clinically, but in such cases there should be the characteristic nodules about the elbows or elsewhere and probably ordinary signs of rheumatoid arthritis. Knuckle pads are not rarely associated with Dupuytren's contracture or the allied condition of acquired camptodactylia.

Reference

Weber, F. Parkes (1938): *Brit. J. Derm.*, 50, 26.

F. PARKES WEBER, M.D., F.R.C.P.

The "Sweating Sickness"

QUERY.—In "The Reign of Edward VI" by James Antony Froude (London, 1926) the author mentions on page 213 "a strange and peculiar plague of the English nation" of that time, called "The sweating sickness, the most mortal of all forms of pestilence which have ever appeared in this country", and which is said to have "selected its victims exclusively from among the natives of Great Britain. If it broke out in a foreign town, it picked out the English residents with undeviating accuracy". What is this "sweating sickness" supposed to be, and, if the observation as to its selective power to attack people of English stock exclusively be correct, what accounts for this?

REPLY.—The cause of the sweating sickness is unknown. The malady first broke out in England in 1485, with subsequent clear-cut epidemics in 1507, 1517, 1528 and 1551. The fifth, and final, sweat is the one described by Froude. The onset of the attack was sudden, with shivering, fever, delirium, prostration, and heavy "stynking" sweats; sometimes "black spots" appeared in the skin, presumably petechiæ. Relapses are mentioned. The sweat was clearly differentiated from bubonic plague and other epidemic diseases of the time. It was not influenza. The

usually average abilities. An experienced doctor will easily recognize in these traits potent factors in the precipitation of the patient's symptoms and in a few minutes of explanation may be able to point the way to relative freedom from attacks. Medicinally, phenobarbitone or Gower's mixture taken regularly for months or even years is of the greatest value in reducing the frequency and severity of attacks. For the relief of the actual attack ergotamine tartrate is the only remedy which holds any prospect of bringing dramatic relief. Given early in an attack, either by mouth in dosage of 2 mgm. or intramuscularly in dosage of 0.25 to 0.50 mgm., it often relieves in a matter of minutes, but when an attack is well established, œdema in the wall of pericranial or intracranial arteries and prolonged spasm of muscles of the scalp and neck may reduce its efficacy. In some patients ergotamine tartrate either causes unpleasant side-effects or consistently fails to relieve. In the former group the administration of oxygen or atropine is often of value, whilst for the latter there is nothing better to offer than the older remedies of aspirin, phenacetin and codeine, and rest in a darkened room.

When headache is due to hypermetropia or astigmatism the wearing of correct spectacles will invariably relieve, and in a proportion of suggestible neurotics spectacles may also bring relief even when the refractive error is insignificant and unrelated to the symptoms.

SINUSITIS

The management of cases of nasal sinusitis calls for much experience and judgment. Nearly every acute case will resolve completely without any treatment and there is rarely any justification for surgical measures, although headlight baths, menthol inhalations and instillation of nasal drops containing ephedrine and penicillin, as well as systemic penicillin and sulphonamides by mouth, may hasten the disappearance of symptoms, whilst aspirin will temporarily alleviate the headache. In cases of *chronic nasal sinusitis* when the nasal septum is grossly deflected, its submucous resection is a simple and minor procedure which is often of the greatest value, whilst radical antrostomy is occasionally necessary. Operations on the frontal sinus are usually most unsatisfactory and seldom to be advised.

HYPERTENSION

The headache of hypertension, especially that associated with hypertensive encephalopathy, is almost always relieved by venesection, although lumbar puncture, or pyretotherapy, or the intravenous injection of 50 c.cm. of 50 per cent. glucose, or the rectal administration of six ounces of 30 per cent. magnesium sulphate solution may be necessary or even preferable if any anæmia is present.

THE NEURALGIAS

Migrainous, ciliary and trigeminal neuralgia are all best treated with simple sedatives and analgesics in the first instance, because in the latter disease long spontaneous remissions are common, especially in its early stages, and because in the former two conditions no therapeutic measure offers certain prospect of relief. The time may arise in all three conditions when alcoholic injection of the Gasserian ganglion should be carried out, and in trigeminal neuralgia it often brings the magical relief that the patient has prayed for. In ciliary and migrainous neuralgia its value is less certain, and in ciliary neuralgia desensitization with histamine or the administration of benadryl or anthisan is often more efficacious.

INJURIES AND NEOPLASMS

In *post-traumatic headache*, when the headache is due to traction on the dura by adhesions, encephalography may prove curative by separating the adhesions.

When headache is produced by *space-occupying lesions* within the skull causing

are often true physical readjustments; e.g., in patients with flexion contracture of the hip or a short leg: more commonly they are the mirror of psychological maladjustment, particularly when associated with pain. It is fashionable to call such disturbances psychosomatic (with emphasis upon the prefix), but obviously all aspects must be given due weight in diagnosis and treatment. The differential diagnosis depends upon what is meant by "obvious radiological abnormality" and upon the viewpoint of the observer. The following is not meant to be a systematic classification nor is it complete.

(1) *Tuberculous disease*.—Often overlooked by those seeking obvious radiological signs but more often not X-rayed at all until later. It should be remembered that a negative skiagram may be positive in two or three months' time and should be repeated if clinical signs suggest it.

(2) *Adolescent kyphosis dorsalis* (late "rickets").—Whatever may be the opinion on the theories of Scheuermann and Schmorl, this condition (and the onset of early osteoarthritis) is clearly a manifestation of relative oversteering of "material" and is often related to defects elsewhere, e.g., tight hamstring muscles (Lambrinudi).

(3) *Congenital malformations of the spine*.—Those causing kyphosis and scoliosis may be outside the dorsal area, e.g., the anomalies of the lumbosacral or cervical regions.

(4) *Neurological disturbances*.—Deformities, the sequel of anterior poliomyelitis. Also such less well-recognized lesions as the kyphoscoliosis associated with a certain form of von Recklinghausen's fibromatosis, with pigmentation and skin nodules.

(5) *Compression lesions of vertebral bodies*.—Calvé's and Kummell's diseases are rare, but compression fractures with all degrees of wedging are common. Neoplastic collapse, either primary or secondary, is uncommon in the third decade.

(6) *Secondary static deformities*.—Some have already

been mentioned, others are related to metabolic and endocrine disturbances. Intrathoracic lesions, particularly the pulmonary causes of kyphoscoliosis, should not be forgotten; nor of course should the heavy massive bosom (macromastia).

The following references are worth consulting:—

- Brailsford, J. F. (1944): "The Radiology of Bones and Joints," 3rd edition, London.
 Goldthwaite, J. E., et al. (1945): "Body Mechanics," 4th edition, London.
 Lambrinudi, C. (1934): *Brit. med. J.*, ii, 800.
 Schmorl, G., and Junghans, H. (1932): "Die Gesunde und Kranke Wirbelsäule im Röntgenbild," Leipzig.
 Wiles, P. (1937): *Lancet*, i, 911.
 N. L. CAPENER, F.R.C.S.

Pethidine-Hyoscine-Trilene Analgesia

QUERY.—I have been using pethidine with hyoscine for inducing analgesia in labour and have given chloroform for delivery of the head, either naturally or with forceps. I should be grateful if you could tell me whether there are any contraindications to the use of trilene instead of chloroform after pethidine with hyoscine.

REPLY.—As regards pethidine-hyoscine with trilene, the latter is quite satisfactory for analgesia. Trilene is apt to cause rapid respiration when pushed to full anaesthesia. I do not recommend hyoscine to be given, anyhow within four hours of delivery.

FRANKIS EVANS, M.B., B.S., D.A.

PRACTICAL NOTES

Sodium Salicylate in Rheumatic Fever

As a result of his experience with 12 patients (9 adults and 3 children) with rheumatic fever, James Reid (*Quarterly Journal of Medicine*, April 1948, 17, 139) concludes that his observations "strongly suggest that in addition to the well-known relief of symptoms, adequate oral administration of sodium salicylate can really cure the disease". The criterion of cure was the return of the erythrocyte sedimentation rate to normal. In all cases the salicylate was given four-hourly from 6 a.m. to 10 p.m. The adults received 2 gm. each time, and in seven of them this was combined with 2 gm. of sodium bicarbonate. Two of the children were given 1½ gm. each of sodium salicylate and sodium bicarbonate on each occasion, whilst the third only received the sodium salicylate (1½ gm.). "Cure" appeared to depend upon the maintenance of a high plasma salicylate level (i.e. 30 to 40 mgm. per 100 c.cm.). As there was considerable variation in this level, and in the speed of attaining it, it is recommended that, to be effective, salicylate administration should be controlled by frequent estimations of the plasma and urinary

salicylate concentration. From the practical point of view, however, the urinary excretion of salicylate is probably a reliable enough guide, as it is a fairly reliable index of the plasma concentration, and has the advantage of involving a simple technique. Attention is drawn to the fact that, in spite of continued oral administration, both plasma and urinary salicylate levels tend to fall after reaching an initial peak level, and it is suggested that the relapses which sometimes occur during the course of treatment of rheumatic fever with salicylates, are due to this fall in plasma salicylate. Oral administration is considered to be as satisfactory as intravenous administration provided an adequate plasma level is maintained, and it has the advantage of being less likely to produce toxic effects.

The toxic manifestations of sodium salicylate administration have been investigated by J. D. P. Graham and W. A. Parker (*Ibid.*, April 1948, 17, 153) in a group of 40 patients with "rheumatic diseases, acute and chronic" and 30 non-rheumatic convalescent patients. Toxic manifestations occurred in 58 of these, and it was found that "a plasma salicylate level

comfortable classes suffered more severely than the poor. Death was common within a few hours:—"There were some dancing in the Court at nine o'clock that were dead at eleven". It was accepted that any sufferer who survived for twenty-four hours was likely to recover. The outbreaks were short and sharp and the infection spread from place to place, thus giving rise to one popular name, "the Posting Sweat". It was not restricted to England. In 1529 the sweat was widespread on the Continent—Germany, Austria, Switzerland, Poland, Denmark, the Netherlands—often accompanied with heavy mortality, as in Hamburg where it is recorded that 1000 persons died within the month.

Both Creighton ("Epidemics in Britain"), and the *Encyclopædia Britannica* state categorically that the disease was unheard of between 1485 and 1507. This is not so, however, for in 1492 the "Plague of Sweat" (*Plaidh Allais*) is recorded in Ireland—"a strange plague of 24 hours' duration; and anyone who survived it beyond that period recovered. It did not attack infants and little children". The sweating sickness was presumably of the same nature as the French "Picardy sweat". In the usual endemic Picardy sweat, the attacks were milder and the mortality low; but its characters in the many epidemic outbreaks, often of very limited extent, resembled those of the sweating sickness. An epidemic of some severity occurred in France in 1887. Although the earliest known accounts of the Picardy sweat date only from 1718, the infection probably existed long before that date. The "First Sweat" (1485) broke out in London a few weeks after the arrival of Henry VII's mercenaries from Bosworth Field. It is at least interesting that, as Creighton first pointed out, these mercenaries were recruited in the locality where the Picardy sweat was later found to prevail. It is not correct to say that the sweating sickness was "the most mortal of all forms of pestilence which has ever appeared in this country". As a killing disease in England it was far outdistanced by bubonic plague.

LIEUT.-GENERAL SIR WILLIAM MACARTHUR,
K.C.B., D.S.O., M.D., F.R.C.P.

Allergy to Eggs

QUERY.—Can you assist me in the treatment of a patient with the annoying symptom of being unable to cope with the digestion of eggs? Consumption of an egg is followed by a general feeling of discomfort, tightness in the epigastrium, and listlessness, which persist for a variable length of time, and are relieved only when an abnormal diuresis and frequency of micturition become established. Separation of the yolk and white appears to reveal that the

white is the more provocative agent. Cauliflower and spring onions have a similar effect, but it is not difficult to cut these out of a dietary. Eggs are a different matter, however, especially when, as in this case, there is an ample supply and other foodstuffs are so hard to acquire. The patient has been checked over by a good physician and is otherwise well. She is not neurotic by temperament, rather the reverse.

REPLY.—These symptoms are probably due to an allergic sensitivity to the foodstuffs mentioned. Sensitivity to egg white is very common, whereas egg yolk is usually innocuous. The sensitivity can be confirmed in most cases by skin tests. For treatment the most simple measure, and a very effective one, is to give an acid mixture (e.g. dilute hydrochloric acid, 30 minims (1.8 c.cm.) with syrup) in water before each meal. Desensitization by subcutaneous injections can also be carried out, but often fails. The desensitizing solution may be obtained from C. L. Bencard, Gorgate Hall, Dereham, Norfolk. Finally, oral desensitization may be tried. The technique will be found in all large textbooks of allergy. The principle is to begin with small doses of diluted egg white and increase daily until a whole egg is taken. The results can be stated as fair.

C. J. C. BRITTON, M.D.

Spinal Deformities in the Third Decade

QUERY.—Kyphosis and scoliosis, without obvious radiological abnormality, and in which early ankylosing spondylitis can be excluded, are often met with in patients in the third decade. Many of these cases would appear to fall into the category of postural deformities: there is localized but rather vague pain and tenderness, and the cases with kyphosis are not corrected with suspension from the horizontal bar. My impression is that the majority of these patients are mentally maladjusted. Could you give me the differential diagnosis of this group, and the name of some textbook dealing with the clinical radiological aspects?

REPLY.—As implied in the question, this is essentially a "fatigue" problem: which signifies either, physically, the relative overstrain of an unsuitably constructed or an unduly weakened "material", or, psychologically, the maladjustment engendered by these physical factors or by external social conditions, as well as by mental states arising primarily. In the pathology of the locomotor system, the third decade of life is a particularly vulnerable period; it is, for example, the period of greatest incidence of spinal tuberculosis; during it the normal ageing processes in joints begin. Postural deformities

course of pregnancy and the puerperium, and it was not until some weeks or months after the cessation of lactation that a return to normal occurred. In view of the definite contrast between the veins in the breasts of pregnant and non-pregnant women, an attempt was made to discover whether the test might be of value in the early diagnosis of pregnancy. In 54 cases in which a definite diagnosis of pregnancy was made on the basis of the infra-red photograph of the breasts, in only one was the diagnosis subsequently found to be wrong. Unfortunately, the converse results were not so satisfactory: i.e., in 17 cases in which the decision on infra-red photograph was against pregnancy, this proved to be correct in only twelve. An impression was gained that in patients who were threatening to abort, the changes were less marked than those in normal pregnancy. In the case of the veins of the legs, an interesting observation was that no change could be demonstrated in them in under four to five months, and the change, once it appeared, did not seem to be altered by the duration of the pregnancy. Similarly, in the abdominal wall, the changes in the veins were not marked, and did not appear until the fifth month or later.

Penicillin in the Treatment of Acute Thromboangiitis

A REPORT of two cases of acute septic thromboangiitis in which penicillin therapy was employed with satisfactory results is given by H. Lux and L. Mangeney (*Presse Médicale*, May 29, 1948, 56, 374). Both cases treated were men, aged thirty-one and forty-eight years respectively. In the first case the patient was admitted with a staphylococcal infection and severe right ilio-femoral obliterating arteritis. There was severe pain, the leg was cold and purple in colour, and oscillations were abolished in the entire length of the limb. Penicillin, which had been given in dosage of 800,000 units daily, was increased to 1,600,000 units, and in five days there was complete cure of the thromboangiitis. The total dosage of penicillin was 34,800,000 units, non-crystallized, over a period of forty-three days. There were no signs of intolerance apart from an urticarial eruption towards the end of the period of penicillin therapy. The patient left the clinic on the sixty-sixth day with a normal leg, with oscillations only slightly diminished, and resumed work one month later. In the second case the patient had a myocardial infarct confirmed by electrocardiographic examination. This patient received 1,600,000 units in twenty-four hours, in divided doses three-hourly, by intramuscular injection: total dosage in thirty-two days,

51,200,000 units of non-crystallized penicillin. He left the clinic on the fifty-eighth day, free of fever, with a normal sedimentation rate, and a satisfactory functional cardiac condition.

Pregnancy and Peptic Ulcers

It is well recognized that peptic ulcers seldom develop during pregnancy and that they rarely become active during pregnancy in patients who have previously had such an ulcer. The reason for this is still obscure, some ascribing it to diminished gastric acidity during pregnancy, others to hormonal influences. In reporting four cases of peptic ulceration occurring during pregnancy or the puerperium, S. P. Bralow *et al.* (*American Journal of Digestive Diseases*, May 1948, 15, 137) draw attention to the danger of misdiagnosis unless it is realized that, although relatively rare, such cases do occur. Of the four cases recorded, two occurred during pregnancy and two during the puerperium. The two patients in whom signs developed during pregnancy had a previous history of a peptic ulcer, whereas there was no such history in the two patients in whom the condition developed during the puerperium. In both these latter women a severe hæmatemesis occurred between the fifth and tenth post-partum day. It is concluded that "obstetricians should not feel safe in view of the reported rarity of the coexistence of peptic ulcer and pregnancy, but should study carefully all cases of persistent heartburn, epigastric distress, etc., in their patients, as peptic ulcers may produce serious complications during or shortly after pregnancy".

Concealment of Skin Blemishes

For the protection of the skin and the disguise of defects the following paste is recommended by A. W. Stillians (*Archives of Dermatology and Syphilology*, February 1948, 57, 279):—

Red ferric oxide.....	6 per cent.
Yellow ferric oxide.....	8 per cent.
Titanium dioxide.....	86 per cent.

The base is a bentonite jelly made by adding 10 gm. of sifted bentonite to 75 c.cm. of stronger rose water, to which has been added 0.5 c.cm. of liquefied phenol. After a jelly has formed on standing, this is slowly added with trituration to 15 gm. of the above powder, to make a smooth paste. Hardening is liable to occur in time owing to loss of water, but this can be overcome by rubbing the moistened finger over the surface. In covering power titanium dioxide is said to surpass zinc oxide, and it is claimed that "an extremely thin coating of this preparation is sufficient for protection of the skin from light or for the concealment of blemishes". To obtain the desired shade the proportions of red and

of 35 mgm. per 100 c.cm. occurring in the first seven days of salicylate therapy appears to be the point above which the more alarming toxic symptoms appear". One case of fatal generalized hæmorrhage occurred in a forty-one year old woman with rheumatoid arthritis who received 10 gm. of sodium salicylate in 1 litre of normal saline intravenously, daily for four days, followed by 10 gm. of sodium salicylate and 10 gm. of sodium bicarbonate daily by mouth. Death occurred on the second day of oral administration. It was found that the occurrence of tinnitus, deafness, nausea and transient vomiting indicated that the plasma salicylates were approaching 35 mgm. per 100 c.cm. The vomiting induced by sodium salicylate is attributed to a central action, although a local irritant action on the stomach is probable. Hyperventilation, which is controlled by the simultaneous administration of sodium bicarbonate, is attributed to reflex stimulation of the respiratory centre through the afferent fibres of the vagus nerve.

Swimming Pool Infections

A SURVEY has been made by J. Roswell Gallagher (*New England Journal of Medicine*, June 24, 1948, 238, 899) in an American boarding school of the incidence of respiratory infections and infective diseases occurring among the boys using the school swimming pool and those who did not use it. The survey covers the years 1941-47 and is limited to the winter term in each year. The swimming pool was equipped with a filtration and chlorination system, and the chlorine level, reaction and bacterial content were determined regularly and always "maintained at highly satisfactory levels". There was a slightly larger number of hospital admissions per boy on account of respiratory illness among the swimmers, as compared with the non-swimmers, the average number of admissions for the seven years being about 14 per cent. greater for the swimmers than for the others. Common colds and acute pharyngitis were 10 and 20 per cent. respectively more prevalent among the swimmers, but the relative frequency among the swimmers and non-swimmers of influenza and hæmolytic streptococcal pharyngitis varied considerably from year to year. There was no difference in the incidence of otitis media in the two groups. The general incidence of chickenpox and scarlet fever in the school was low during the period covered by the investigation, but in the case of both these diseases the incidence was higher among non-swimmers than among regular swimmers. On the other hand the incidence of mumps and measles tended to be higher among the swimmers. The conclusion is drawn that "when careful control is exercised and when normal

conditions exist, there is no reason to expect a higher incidence of respiratory infection among swimmers. In the presence of a highly communicable disease, however, these data suggest that it is desirable to take extra precautions in this group mumps and measles seemed to spread more rapidly among the swimmers".

Oral Penicillin in Pediatrics

THE following are the main conclusions reached by J. H. Moseley (*Archives of Disease in Childhood*, June 1948, 23, 93) from an investigation, in Birmingham, of the absorption of penicillin from the alimentary tract of forty infants.— "As a result of this work it is claimed that penicillin may be administered orally to any infant below the age of six months as reliably as the sulphonamides, provided a big enough dose is employed and mixed feeding has not been started. It is not agreed that injection is the route of choice in severely ill babies. It is just in these cases that the full advantages of oral administration are apparent. Where there is persistent vomiting or severe enteritis, parenteral administration must be employed. The relaxed undigested stools so frequently seen in the course of infection in infancy are not a contraindication to giving the drug by mouth. Further, it was found that the modification of the feed by lactic acid does not destroy the penicillin. The size of the dose must be based on the age and not the weight of the infant. This rule applies to premature babies as well". The doses employed were as follows:—

Age	3-hourly	4-hourly
0-6 weeks	20,000 units	30,000 units
6 weeks to 3 months	40,000 units	60,000 units
3 months to 6 months	50,000 units	70,000 units

"These doses are given immediately before each feed. At night a double dose is given before the last feed . . . In no case have any toxic manifestations been observed".

Infra-Red Photography in Pregnancy

THE well-known property of infra-red photography of demonstrating the superficial veins has been utilized by Kenneth Bowes and his colleagues (*Journal of Obstetrics and Gynecology of the British Empire*, June 1948, 55, 285) to study the changes which occur in the superficial veins during pregnancy, particularly in the breast. In all, 115 patients were photographed. In the breasts, changes were noted as early as the 3rd or 4th week of pregnancy, and were usually marked by eight weeks. Gravity appeared to have little effect on these changes, which consisted of an increase in the number of veins, their density and their anastomoses. The veins became more marked during the

REVIEWS OF BOOKS

Human Nutrition. By V. H. MOTTRAM, M.A. London: Edward Arnold & Co., 1948. Pp. 151. Figures 9. Price 6s. 6d.

A LIFETIME spent in the teaching of dietetics, a pleasantly caustic pen, and a generous helping of common sense combine to make this one of the best textbooks of dietetics that has yet been published. Written primarily for dietiticians in training, it manages to cover the whole field, with the emphasis throughout on the more practical aspects of the subject. Thus, whilst the physiological aspects of nutrition are dealt with, no time is wasted on details, just as in dealing with the vitamins only sufficient theoretical information is provided to permit of the reader understanding the practical implications. Like all experts in nutrition and dietetics, the author has his pet bees in his bonnet, but, unlike too many of his fellow-nutritionists, he never allows them to buzz too loudly. Now and again curious statements creep in, such as the one that brain is "not very digestible or absorbable", but few such lapses are to be found. The strain in which the whole book is written is well exemplified in the following quotation: "In general, the nutritionist is mildly contemptuous of processes that waste quite a percentage of the food values of cereals, grape and apple-juice, etc., in order to make expensive beverages of a doubtful dietetic value, however pleasant they may be"! This is a book which is a joy to read and which can be thoroughly recommended to all who are interested in nutrition and dietetics. Students, both medical and dietetic, will find it particularly useful.

Surgery of the Colon and Rectum. By SIR HUGH DEVINE, M.S., F.R.C.S., F.R.A.C.S., F.A.C.S., and JOHN DEVINE, M.S., F.R.A.C.S., F.A.C.S. Bristol: John Wright and Sons Ltd., 1948. Pp. xi and 373. Figures 277. Price 52s. 6d.

No man alive to-day has made contributions to the surgery of the colon and rectum comparable with those of Sir Hugh Devine of Melbourne. In 1928 he extended the principle of exteriorization, first enunciated by F. T. Paul of Liverpool in 1895, to the resection of growths of the right side of the colon. He followed by introducing temporary excluding transverse colostomy as a preliminary to colectomy and primary suture in a defunctioned distal colon. In 1937 he described synchronous combined abdomino-perineal resection of the rectum by two surgeons; an operation that has since replaced all others in most parts of the

world. He now describes a method of resection of the rectum with preservation of the anal sphincters that appears to be safer, both from the point of view of sepsis at the time and of recurrence afterwards, than any other published technique of this controversial operation. In addition to these advances in principle, he has introduced a new technique in abdominal surgery, that of working in a field from which all viscera but those that immediately concern the surgeon are excluded by a series of mechanized hands attached to an operating frame. He has also invented a number of ingenious instruments. In this book Sir Hugh, writing with his son John, has given us a comprehensive review of the whole of large intestine surgery. The introductory sections on anatomy and physiology are excellent; the descriptions and illustrations are admirably clear. The book has all the merits of one that is unashamedly, indeed triumphantly, personal, in that the authors know exactly what they mean, and say it clearly and dogmatically. Some personal foibles, such as the use of the obsolete word "clyisma" for "enema" may irritate, and there are a few errors in the text, but the book is a classic and should be read by all surgeons who are ever likely to work in the abdomen.

Cardiography. By WILLIAM EVANS, M.D., D.Sc., F.R.C.P. London: Butterworth & Co. (Publishers) Ltd., 1948. Pp. ix and 140. Figures 211. Price 25s.

This book deals with electrocardiography and phonocardiography. It replaces the author's primer on electrocardiography which was so popular before the 1939-45 war. Written with that simplicity of style and clarity of thought which characterize all the publications of the Cardiac Department of the London Hospital, it is a model of how such a manual should be produced. The standard of reproduction of the many electrocardiograms and phonocardiograms is equally high. Intended primarily for the beginner, it will be of equal value to the senior student, the postgraduate working for a higher diploma, the house physician and the practitioner. All the common conditions encountered in practice are reproduced here, and a useful addition is a section in which a series of electrocardiograms are included without any accompanying legends. The legends are printed together in a later section of the book. In this way the reader is provided with a series of "test electrocardiograms" by which he can assess his ability to provide a correct interpretation. The only criticism to be offered is of the legends to the electrocardiograms; the

yellow oxides may need to be altered. One of the advantages of this paste is said to be that there is relatively little danger of sensitization.

Renal Decapsulation for Sulphathiazole Anuria

RENAL damage due to the sulphonamides has been divided into two main groups: (a) mechanical obstruction due to crystalline deposition; (b) toxic intra-renal lesions without obstruction. For the treatment of this latter group I. J. Shapiro (*Journal of Urology*, April 1948, 59, 528) recommends bilateral decapsulation of the kidneys should all other measures fail. Emphasis is laid upon the fact that in cases of anuria due to the toxic action of the sulphonamides there is no time for temporization. Cystoscopy and ureteral catheterization should be done at once to determine whether or not the anuria is due to deposition of crystals. Even though no such evidence is obtained pelvic lavage should be carried out with bicarbonate solution. If the anuria still persists, bilateral renal decapsulation is recommended to be carried out without further delay. If this is not performed in such cases at a relatively early stage, irreversible changes may occur in the renal parenchyma. It is claimed that decapsulation carries with it practically no primary mortality and that it can be performed rapidly under local or regional anaesthesia, even in very toxic individuals. In support of the thesis, two cases are reported in which complete recovery ensued following bilateral decapsulation.

Treatment of Haemophilia

BASING their conclusions upon a series of 43 haemophilic subjects, Claude-Starr Wright *et al.* (*Journal of Laboratory and Clinical Medicine*, June 1948, 33, 708) consider that measures are now available which permit "in the individual patient with haemophilia both emergency and elective surgical procedures, with relative safety". These measures consist of the intravenous or intra-marrow administration of fresh whole blood or plasma, reconstituted frozen plasma, or plasma fraction I of Cohn. If there has been much loss of blood, fresh whole blood or plasma should be given. Frozen plasma is prepared by prompt separation of all cellular elements from blood, followed by a rapid freezing of the whole plasma within a few hours after withdrawal from the donor. In the frozen state the anti-haemophilic activity of normal human plasma remains potent indefinitely. For restitution of this frozen plasma, rapid thawing is necessary in a water bath at 37° C. The activity of thawed plasma diminishes rapidly after several days' storage at

4° C. Fifty cubic centimetres of either fresh or reconstituted frozen plasma given intravenously is said to maintain the coagulation time within safe limits for approximately twenty-four hours in a moderately severe haemophilia. The anti-haemophilic fraction of human plasma (plasma fraction I of Cohn) is dissolved in distilled water, and has an anti-haemophilic activity of ten to fifteen times the comparable volume of plasma from which it was obtained. It also is given intravenously. In the case of child haemophiles the veins may be difficult to find, and in such cases intra-sternal or intra-tibial infusions are equally satisfactory. Whilst these general measures are usually sufficient if initiated before operation and maintained for several days postoperatively, it is often advisable to use haemostatic agents at the site of operation to control haemorrhage. The most effective of these are fibrin foam and thrombin.

Papaverine in Cerebral Angiospasm

THE use of papaverine hydrochloride in a series of forty-six patients with encephalopathy associated with hypertensive disease, and in cerebral vascular disease without hypertension is recorded by H. I. Russek and B. L. Zohman (*Journal of the American Medical Association*, April 3, 1948, 136, 930). The drug was given orally in dosage varying from 4½ grains (0.29 gm.) to 12 to 18 grains (0.75 to 1.2 gm.) daily, according to the individual requirements of the patients, in three or four divided doses, in conjunction with phenobarbitone, ½ to 1 grain (16 to 32 mgm.). In two patients who had suffered for a number of years from frequently recurring cerebral attacks there was complete disappearance of symptoms after treatment. The drug was also found effective in decreasing the severity and frequency of seizures in some cases of advanced malignant hypertension. No untoward effects of the drug were noted, even in the cases in which high dosage was employed.

A Radiological Sign of Retroperitoneal Abscess

BASING their report on two cases of retroperitoneal abscess due to a ruptured retroperitoneal appendix, G. C. Bird, Jun. *et al.* (*American Journal of Roentgenology*, March 1948, 59, 351) describe a radiological sign which they claim to be of value in the diagnosis of retroperitoneal abscess. This consists of "multiple small radiolucent shadows" in the retroperitoneal space. These multiple small gas shadows are said to be present early in the disease. Their detection and accurate localization are facilitated by stereoscopic posterior or oblique films.

A Handbook of Ophthalmology, by Humphrey Neame, F.R.C.S., and F. A. Williamson-Noble, F.R.C.S., in its sixth edition (J. & A. Churchill Ltd., 21s.) contains among the new additions a section on the use of penicillin in the treatment of conjunctivitis and its administration in the form of eye-drops and ointments. Mention is also made of the use of benadryl in the treatment of penicillin allergy. New information on the chemistry of myosis and mydriasis and the pathology of diabetic retinopathy are other welcome additions.

Textbook of Anæsthetics, by R. J. Minnitt, M.D., D.A., and John Gillies, M.B., Ch.B., F.R.C.S., D.A., in its seventh edition (E. & S. Livingstone Ltd., 30s.) contains a new chapter on curare, in which its mode of action, pharmacology, and methods of administration are described in detail. Advances in regional analgesia, a section on pethidine chloride in the chapter on analgesia and anæsthesia in obstetrics, and a new chapter on legal aspects are other welcome features of the new edition.

EXTENSIVE revision to include the many advances in therapeutics during the eight years

that have elapsed since the appearance of the previous edition has been undertaken in the preparation of the thirteenth edition of *An Index to Treatment*, edited by Sir Robert Hutchison, Bt., M.D., F.R.C.P. (John Wright and Sons, Ltd., 84s.). Chemotherapy looms large among the new additions. This well-known guide to treatment has been brought up to date in all sections.

Clinical Electrocardiography, by David Scherf, M.D., F.A.C.P., and Linn J. Boyd, M.D., F.A.C.P., in its third edition (Wm. Heinemann [Medical Books] Ltd., 30s.) has been subjected to complete revision and a number of new figures added. The value of the chest leads in the diagnosis of myocardial infarction, bundle branch block, and cardiac hypertrophy is stressed, and also of the unipolar limb leads in posterior wall infarction.

The Care of Tuberculosis in the Home, by James Maxwell, M.D., F.R.C.P., in its second edition (Hodder and Stoughton, 7s. 6d.) has not been subjected to any extensive revision. The title explains the nature of the book, and much useful information will be gained from its perusal.

NOTES AND PREPARATIONS

NEW PREPARATIONS

FERRIVENIN is a 2 per cent. saccharated iron oxide preparation for intravenous administration in refractory hypochromic anæmia. It is issued in ampoules of 5 c.cm., each containing 100 mgm. of metallic iron. The manufacturers are Benger's Ltd., Holmes Chapel, Cheshire, from whom clinical samples and literature can be obtained.

NITROGEN MUSTARD HYDROCHLORIDE—Boots—(di-(2-chloroethyl) methylamine hydrochloride) is issued in vials of 10 mgm., in boxes of 10, for use in the treatment of Hodgkin's disease, leukemia, polycythæmia, and certain neoplastic diseases. The manufacturers are Boots Pure Drug Co., Ltd., Station Street, Nottingham, from whom literature and further particulars can be obtained.

TETRETHYLPHOSPHATE (T.E.P.P.) and **Diisopropylfluorophosphate (D.F.P.)** are now available:—T.E.P.P. in tablets of 1, 2 and 5 mgm., and solution in propylene glycol 5 mgm. per c.cm. for intramuscular injection, in boxes of 12 ampoules of 1 c.cm., and D.F.P. in ampoules of 0.1 per cent. in arachis oil for intramuscular injection, and in an 0.05 per cent. solution in arachis oil for ophthalmic use. The manufacturers are Allen & Hanburys Ltd., Bethnal Green, London, E.2.

A SIMPLE METHOD OF TESTING THE URINE FOR SUGAR

CLINITEST, produced by the Ames Company Incorporated, is a simple method of testing the urine for sugar which dispenses with the need for a spirit lamp or similar source of heat.

A tablet of the reagent, which contains copper sulphate, is added to five drops of urine diluted with ten drops of water in a test tube, and on dissolving sufficient heat is produced spontaneously to boil the solution, which gives colour changes similar to those obtained with Benedict's solution.

The testing outfit is available in a small bakelite case containing test tube, pipette, a bottle of tablets and colour matching card, price 12s. The whole apparatus is of small dimensions and can be carried in the pocket. The sole distributors for the British Isles are Don S. Momand Ltd., 57 Albany Street, London, N.W.1.

BRITISH EMPIRE CANCER CAMPAIGN

AMONG the many facts of interest contained in the Twenty-Fifth Annual Report of the British Empire Cancer Campaign, covering the year 1947, are particulars of the use of nitrogen mustard, radio-active phosphorus (P^{32}), radio-zinc (Zn^{65}), and urethane. The work of Professor Dadds on the synthesis of stilbæstrol and its use in the treatment of carcinoma of the prostate has been recognized by the award of the Garton

absence of any heading to these is a disadvantage which outweighs the advantages claimed for the system. This, however, is an excellent work, upon which the author is to be congratulated.

Bilharzial Cancer: Radiological Diagnosis and Treatment. By M. A. AFI, M.B., Ch.B., M.R.C.S., L.R.C.P., D.M.R.E. London: H. K. Lewis & Co., Ltd., 1948. Pp. viii and 111. Figures 60. Price 16s.

THIS book is based on the author's clinical and radiological experience over a period of twenty-five years in Egypt. Part I reviews the association of bilharziasis with cancer in various organs. Autopsy reports from the main pathological centres of Egypt indicate that about 24 per cent. of carcinomas are associated with bilharziasis. Only in the bladder and colon is this association of the two diseases sufficiently great to suggest causal relationship, e.g., in 92 out of 94 autopsies, carcinoma of the bladder was associated with bilharziasis. The significance of the term bilharzial cancer is discussed on the basis of information supplied at autopsy; the author concludes that in Egypt, where bilharziasis affects 30 to 90 per cent. of the population, "it is not strange that when malignant disease starts to develop for any reason it finds an already existing bilharzial infection". The conception of bilharzial cancer can only be justified in the general sense of the close association of the two diseases. The second part of the book deals with the radiological diagnosis of bilharziasis of the urinary and intestinal tracts, especially when associated with cancer. This section is well illustrated by clear skiagrams, and contains a number of case reports. Part three is concerned with treatment, which is considered mainly from a radiotherapeutic point of view. There is a short bibliography. The material is well presented, except for some minor errors in phraseology. This is a readable little book and will be useful to those clinicians who have to deal with bilharzial infections.

Bacterial and Virus Diseases. By H. J. PARISH, M.D., F.R.C.P.Ed., D.P.H. Edinburgh: E. & S. Livingstone Ltd., 1948. Pp. 168. Illustrated. Price 7s. 6d.

THIS book, although quite small, contains a great deal of information. It deals with the subject of immunity, and with antisera, toxoids, vaccines and tuberculin in prophylaxis and treatment. The methods of immunization against diphtheria, scarlet fever, tetanus and other diseases are carefully described. There is also a summary of the more important dates in the modern development of serum therapy and

prophylaxis by active immunization. A valuable feature is the advice given as to the keeping qualities of sera and methods of storage. This is essentially a practical book and should prove a welcome addition to the library of a clinical laboratory or of the public health department of a municipality.

Epilepsy. EDITED BY PAUL H. HOCH, M.D., and R. P. KNIGHT, M.D. London: Wm. Heinemann (Medical Books) Ltd., 1948. Pp. vii and 214. Illustrated. Price 21s.

THIS work comprises fifteen papers on different aspects of epilepsy, from "The Proceedings of the Thirty-Sixth Annual Meeting of the American Psychopathological Association, held in New York City, May, 1946". It will appeal mainly to neurologists, psychiatrists, pathologists and sociologists, but the general practitioner who is interested in epilepsy will also glean much information from these authoritative articles on various facets of the subject. Among the chapters of general interest are a brief but admirable historical sketch on epilepsy, an historical review of the pharmacological approach to treatment, an essay on social implications and management, and a summing up on the important advance in the knowledge of the epilepsies afforded by the use of the electro-encephalogram.

Breast Feeding. By F. CHARLOTTE NASH, M.B., B.C. London: Oxford University Press, 1948. Pp. xii and 151. Figures 20. Price 10s. 6d.

THE decline of breast feeding is causing alarm. The general standard of management is poor. Dr. Nash's excellent little book describes in simple language the physiology of lactation and the management of breast feeding. It is practical and based on wide experience in general practice and at home. It should be read by general practitioners, health visitors, and nurses concerned with child welfare; also by the more intelligent type of expectant mother.

NEW EDITIONS

Two new chapters, on cysts of the lung and pleura, and on sarcoidosis, have been added to *A Practical Manual of Diseases of the Chest*, by Maurice Davidson, M.D., F.R.C.P., in its third edition (Oxford University Press, 50s.), and the chapter dealing with the pneumonokonioses has been revised and enlarged. Penicillin and the sulphonamides in the treatment of pneumonia, new information on tuberculous tracheo-bronchitis, mass radiography, and a number of new illustrations are among the features of the new edition, which is beautifully produced.

THE PRACTITIONER

No. 964

OCTOBER 1948

Volume 161

ADVANCES IN MEDICINE

By HENRY COHEN, M.D., F.R.C.P.

Professor of Medicine, University of Liverpool; Senior Physician, Royal Infirmary, Liverpool.

"In the track of great armies there must follow lean years".

Sayings of Lao Tze.

"Every solution of a problem is a new problem".

Goethe.

THE year which has just passed may well be accounted one of the most momentous in the annals of medical history for it has given birth to an experiment in social medicine on a national scale, which, if successful, will rightly claim to be regarded as the greatest advance in medicine in our time. Yet it has witnessed no novel discovery in medical science which can be compared with that of penicillin. Much earlier knowledge has been consolidated and expanded; new techniques have been developed; orientations have been modified and emphases have changed. Methods have been recorded for increasing the potency of penicillin; new antibiotics have been developed which are effective against penicillin-resistant organisms; promising chemotherapeutic agents in the treatment of tuberculosis have been described; the results of planned war-time research have been successfully applied to the medical problems of peace; surgery, especially in cardiovascular disease, has become bolder and safer; antithyrototoxic and antihistamine drugs have found a secure place in therapeutics; and the interaction of body and mind in the genesis of disease, and the social and economic implications of illness have been increasingly recognized. The ensuing review confines itself to a few of the more important topics which lie on the growing edge of medicine, especially of therapeutics.

PENICILLIN

It is not unnatural, nor does it detract from the inestimable value of penicillin, that much recent work has stressed some of its shortcomings. Toxic reactions remain very rare, although such allergic responses as urticaria, dermatitis, fever, and even neuritis are recorded, probably due to impurities. There is, however, some experimental evidence which suggests that the pure crystalline forms of penicillin are less effective against experimental streptococcal and pneumococcal infections than are the less pure preparations.

Medal and Prize. The address of the British Empire Cancer Campaign is 11 Grosvenor Crescent, Hyde Park Corner, London, S.W.1.

NEWTON VICTOR LIMITED

ON July 31 a new company, Newton Victor Limited, came into being, amalgamating Victor X-ray Corporation Ltd., Newton & Wright Ltd., and the X-ray research and manufacturing activities of Metropolitan-Vickers Electrical Company Ltd. Newton Victor Limited is a wholly British enterprise devoted to the design, production, distribution and servicing of X-ray and associated equipment. The head office is at 15 Cavendish Place, London, W.1.

MEDICAL AUXILIARY SERVICES

THE sixth edition of *The National Register of Speech Therapists* has recently been issued. A Speech Therapy Conference will be held from September 20-24, 1948, at the Royal Society of Medicine, 1 Wimpole Street, London, W.1. Particulars can be obtained from the College of Speech Therapists, 68 Queen's Gardens, London, W.2. The eighth edition of *The National Register of Orthoptists* has also been issued. Practitioners can obtain copies of these Registers, free of charge, on application to the Registrar, Board of Registration of Medical Auxiliaries, Tavistock House North, Tavistock Square, London, W.C.1.

PUBLICATIONS

British Hospitals, by A. G. L. Ives (Collins, 5s.), is the latest addition to the successful "Britain in Pictures" series. It well maintains the standard of the series in style, typography and illustration. The author, who is secretary of the King Edward's Hospital Fund, has succeeded in presenting a reliable picture of the development of hospitals in Great Britain.

A.B.C. of First Aid Treatment, by Air Marshal Sir Harold Whittingham, a manual of instruction with illustrations, is published by the British Red Cross Society, 14 and 15 Grosvenor Crescent, London, S.W.1.

The Medical Directory. Messrs. J. & A. Churchill Ltd., write:—

"To maintain the accuracy of our annual volume we rely upon the return of our schedule, which has been posted to each member of the medical profession. Should the schedule have been lost or mislaid we will gladly forward a duplicate upon request".

J. & A. Churchill's "Complete List of Current Publications, June 1948", has just been issued and can be obtained on application to 104 Gloucester Place, London, W.1.

OFFICIAL NOTICES

National Health Service Act, 1946: Compensation to Doctors for the Loss of the Right to Sell the Goodwill of their Practices. Doctors who retired from practice or the personal representatives of doctors who died between the date of the passing of the Act, November 6, 1946, and July 5, 1948, and whose practices have not been sold in whole or part by July 5, 1948, should make early application to the Secretary, Medical Practices Committee, Devonshire House, Mayfair Place, Piccadilly, London, W.1.

National Health Service (Superannuation) Regulations, 1947 and 1948. A booklet entitled "Superannuation Scheme for those Engaged in the National Health Service—An Explanation", and a leaflet (S.D.D.) have been issued by the Ministry of Health. Practitioners are advised to study these before filling the Superannuation form S.D.28.

National (War) Formulary, third edition, 1947. Amendment No. 2 (1948) has recently been issued by the Ministry of Health, and came into operation for National Health Service purposes on August 1, 1948.

Streptomycin: Inquiries by Phone. Under the arrangements of the Ministry of Health for supplying streptomycin for cases of military tuberculosis and tuberculous meningitis, applications by phone should be made to Kensington 3471 ext. 102 (Monday to Friday, 8.30 a.m.-6 p.m.; Saturday, 8.30 a.m.-2 p.m.). At all other times (night and weekends) Whitehall 4300.

Report of the Ministry of Health for the year ended March 31, 1947, can be obtained from H.M. Stationery Office, price 3s. 6d.

Artificial Limbs: Second Report of the Standing Advisory Committee, is obtainable from H.M. Stationery Office, price 4d.

Erratum—In the article on "Asthma", by C. Astley, word "amino" of page 468

Binding Cases for Volume 160 (January—June 1948) in green cloth with gilt lettering are now available, price 4s. post free, from the Publishing Department, *The Practitioner*, 5 Bentinck Street, London, W.1. Subscribers in Liverpool and district may like to send their copies for binding to the Sir Robert Jones Memorial Workshops, 74 Upper Parliament Street, Liverpool, 8.

The contents of the October issue, which will be a special number devoted to "Advances in Treatment", will be found on page lxix at the end of the advertisement section.

THE PRACTITIONER

No. 964

OCTOBER 1948

Volume 161

ADVANCES IN MEDICINE

By HENRY COHEN, M.D., F.R.C.P.

Professor of Medicine, University of Liverpool; Senior Physician, Royal Infirmary, Liverpool.

"In the track of great armies there must follow lean years".

Sayings of Lao Tze.

"Every solution of a problem is a new problem".

Goethe.

THE year which has just passed may well be accounted one of the most momentous in the annals of medical history for it has given birth to an experiment in social medicine on a national scale, which, if successful, will rightly claim to be regarded as the greatest advance in medicine in our time. Yet it has witnessed no novel discovery in medical science which can be compared with that of penicillin. Much earlier knowledge has been consolidated and expanded; new techniques have been developed; orientations have been modified and emphases have changed. Methods have been recorded for increasing the potency of penicillin; new antibiotics have been developed which are effective against penicillin-resistant organisms; promising chemotherapeutic agents in the treatment of tuberculosis have been described; the results of planned war-time research have been successfully applied to the medical problems of peace; surgery, especially in cardiovascular disease, has become bolder and safer; antithyrototoxic and antihistamine drugs have found a secure place in therapeutics; and the interaction of body and mind in the genesis of disease, and the social and economic implications of illness have been increasingly recognized. The ensuing review confines itself to a few of the more important topics which lie on the growing edge of medicine, especially of therapeutics.

PENICILLIN

It is not unnatural, nor does it detract from the inestimable value of penicillin, that much recent work has stressed some of its shortcomings. Toxic reactions remain very rare, although such allergic responses as urticaria, dermatitis, fever, and even neuritis are recorded, probably due to impurities. There is, however, some experimental evidence which suggests that the pure crystalline forms of penicillin are less effective against experimental streptococcal and pneumococcal infections than are the less pure preparations.

The two major problems associated with penicillin therapy are (1) the rapid excretion of the drug, necessitating frequent (four-hourly) parenteral injections if an adequate blood level is to be maintained, and (2) the possible development of penicillin-resistant strains.

The poor absorption of penicillin when given by mouth has been thought to be due to its destruction by hydrochloric acid in the stomach and by penicillinase-producing bacteria in the lower gut, but McDermott *et al.* (1946) showed that achlorhydria did not improve penicillin absorption from the stomach. Stewart and May (1947) stressed that absorption was mainly from the duodenum. They found that provided the oral dose was five to ten times greater than the parenteral dose, adequate blood concentrations of penicillin could be secured. The drug is best given in a small quantity of 5 to 10 per cent. glucose solution, which masks its bitter taste, half an hour before breakfast or four hours after meals, and if necessary, to ensure that the gastric pH is not less than 3.0, sodium bicarbonate or sodium citrate should be given. There are, however, marked individual variations as yet unexplained in the amount of penicillin absorbed.

To try to counter the rapid excretion of penicillin, two measures have been followed. First, an attempt has been made to delay absorption by creating a depot of penicillin from which it is but slowly absorbed; to secure this, solutions in arachis oil and beeswax have had official sanction, but they remain unpopular because they are often difficult to inject, they are not without local discomfort, and their efficacy is doubtful. The more promising measures are those which tend to retard the excretion of penicillin. Experiments show that 20 per cent. of the drug is filtered through the glomeruli and 80 per cent. through the renal tubules, so the problem is essentially one of control of tubular excretion. For this purpose two drugs—diodrast and *p*-aminohippuric acid—which compete with penicillin on a mass action basis for excretion by the renal tubules, have proved impracticable. But recently a third drug—caronamide (4'-carboxyphenylmethanesulphonamide)—has been described which appears to block the specific enzyme transport system responsible for the passage of penicillin through tubular epithelium. Given orally, in doses of 2 to 3 gm. four-hourly, it is rapidly absorbed and does not interfere with blood penicillin assays, nor does it antagonize the sulphonamides when given in their usual dosage. By whatever route penicillin is administered, the simultaneous use of caronamide raises the blood level two to seven times. Caronamide has no intrinsic bacteriostatic effect. There are, as yet, few therapeutic reports on its efficacy, but Loewe *et al.* (1947) reported favourably on 9 cases of subacute bacterial endocarditis treated by combined caronamide and penicillin therapy. As albuminuria, with occasional red cells in the urine but no permanent renal damage, occurred in 8 of these patients, however, the risk of nephritis cannot be overlooked.

There are two aspects of the problem of the development of penicillin-

resistant strains which deserve mention. First, the possibility of mutation of sensitive into resistant organisms, and secondly, the fostering, by elimination of sensitive organisms, of the growth of non-sensitive organisms of the same or other strains. Staphylococci are easily rendered insensitive to penicillin *in vitro*, but organisms so produced rapidly lose their resistance to penicillin when injected into animals. There is, however, some experimental evidence that resistance might develop from the repeated passage of strains through animals, but this is extremely slow (Miller and Bohnhoff, 1945). Widespread interest and anxiety arose from Barber's (1947) report that of 200 strains of staphylococci (99 from infected lesions) examined in 1946, 12.5 per cent. were resistant to 10 units of penicillin in an agar ditch-plate; in 1947, 38 of 100 strains tested (all from infected lesions) proved to be resistant, and it was suggested that this might indicate that there was appearing more frequently a natural resistant strain of staphylococci. But the two groups were not strictly comparable. In the 1947 series, 28 of the 38 resistant strains were from patients who had earlier been treated with large doses of penicillin. More evidence is needed before firm inferences are drawn, and this should include cases examined at the onset of infection and before any antibiotic treatment has been given. But the dangers of breeding resistant strains through treatment, on the analogy of other infections (e.g. arsenic-fast protozoa and sulphapyridine-fast gonococci), must be envisaged, and countered (1) by adequate initial dosage to destroy moderately resistant as well as sensitive strains and so prevent the former from increasing; (2) by the combined use of antibiotics and sulphonamide drugs; and (3), especially when prolonged treatment is necessary, by the avoidance of indiscriminate therapy with antibiotics.

Penicillin in syphilis.—"History may not repeat itself but historical situations recur". Penicillin, like salvarsan, is no *therapia sterilisans magna*. Varying opinions have been expressed on the efficacy of very large doses of penicillin given once or twice daily to out-patients. Most reports show a significant number of failures, e.g. British Army figures reveal that twelve months after giving 2.4 mega units of penicillin the failure rate was 14 per cent. for sero-negative primary cases, 13 per cent. for sero-positive primary cases, and 17.5 per cent. for secondary cases. Most relapses in early syphilis occur within six months of the completion of treatment; therefore, as with arsenical and bismuth therapy, a second course of penicillin is advisable after three months. It is, of course, too early to assess the value of penicillin in preventing the later manifestations of syphilis.

In the prevention of congenital syphilis, penicillin has proved most effective. Speiser *et al.* (1947) report that in treated syphilitic pregnant women, even though treatment is started late in pregnancy and the mother is not always cured, a healthy child is born in 95 per cent. of cases. So also the results in infantile congenital syphilis are excellent. In cardiovascular syphilis the effects are not so striking and the possibility of Herxheimer

reactions cannot be ignored. Although some workers (Martin, 1948) regard penicillin alone as adequate in the treatment of most forms of neurosyphilis, including general paralysis of the insane, others (Worster-Drought, 1947; Lescher and Richards, 1947) recommend in this, as in other forms of syphilis, the combined use of penicillin with arsenic and bismuth; and pyretotherapy, e.g. with malaria, is a valuable adjunct in cases of general paralysis of the insane, taboparesis and primary optic atrophy. In syphilis there are no advantages in intrathecal penicillin; indeed this carries all the risks and discomforts of severe meningeal irritation.

Penicillin and sulphathiazole in typhoid fever and brucellosis.—Following Bigger's experimental studies on the synergic action of penicillin and sulphathiazole against the typhoid group of bacilli, McSweeney (1946) reported dramatic improvement in 6 cases of typhoid fever by giving 10 mega units of penicillin and 34 gm. of sulphathiazole during a four-day period, repeating the course after two days' rest. Treatment started on the tenth day to the third week. Subsequent reports, including those of Parsons (1948) based on experience in many hospitals in the Middle East, and Bevan *et al.* (1948), who treated 39 patients in the Aberystwyth outbreak, failed to confirm the earlier optimistic reports, and there is general agreement that the indiscriminate use of penicillin and sulphathiazole in the treatment of typhoid fever should be condemned. Similar reports concerning the value of combined penicillin and sulphathiazole therapy in undulant fever have appeared, but they lack conviction.

DRUGS AGAINST TUBERCULOSIS

So potent a killing disease as tuberculosis has naturally attracted research into its specific therapy. The agents suggested fall into three groups (Hart, 1946):—

(1) *Synthetic substances with no known counterpart in nature.*—These include derivatives of 4,4'-diaminodiphenyl sulphone, commonly known as the sulphone drugs; of these "promin" (or "promanide"), "diasone", and "promizole" are the best known. It may be said that although these exert measurable therapeutic effects on animals infected experimentally with human tubercle bacilli, they are disappointing in the treatment of human disease. It is, however, interesting to note that they give a most encouraging response in leprosy (Faget *et al.*, 1946).

(2) *Synthetic substances related to naturally occurring compounds.*—The observation that benzoic and salicylic acids increase the oxygen uptake of washed suspensions of tubercle bacilli suggested that substituted similar compounds might interfere with the normal oxidative processes, deamination or enzyme systems of the bacillus. To this end Lehmann (1946, 1948) introduced para-aminosalicylic acid (P.A.S.). Contrary to the experience of others, Feldman *et al.* (1947a) found that the drug was well tolerated by guinea-pigs for a prolonged period of continuous medication, and that even

though low blood concentrations of the drug were recorded, there was unmistakable evidence of a favourable influence on the course of tuberculous infections in guinea-pigs. Limited supplies and high dosage have curtailed clinical trials, but two English series (Dempsey and Logg, 1947; Erdei, 1948) suggest that P.A.S. may prove a valuable adjunct to existing therapeutic measures, and that owing to high concentrations in the urine, it may have a specially beneficial effect on tuberculosis of the urinary tract. Toxic effects include vomiting and diarrhoea, although these are unusual. The drug is given orally in doses of 14 gm. daily (for an adult), divided into four to six doses. It is rapidly absorbed and excreted. A blood concentration of 3 to 6 mgm. per c.cm. should be maintained and treatment continued for several months. Lehmann (1948) found no evidence of bacterial resistance from prolonged administration; he regards the blood sedimentation rate as the most reliable and sensitive index of effective treatment. Dempsey (1948) gives 20 to 30 gm. daily, and reports favourable results from intrapleural P.A.S. in tuberculous empyema when no broncho-pleural fistula exists.

(3) *Substances of biological origin*, especially the antibiotic, streptomycin, isolated by Waksman in 1944, who recognized its action on the tubercle bacillus.

STREPTOMYCIN

In tuberculosis.—In the past four years intensive research, experimental and clinical, has revealed both the value and the limitations of this drug. Feldman and Hinshaw (1948), pioneers in its development, have published a comprehensive survey of the knowledge of its actions, and a special committee of the Medical Research Council has recorded the results of treatment in 105 cases of tuberculous meningitis (1948).

Intensive parenteral and intrathecal streptomycin is advised in *tuberculous meningitis*; 25 to 40 per cent. survive at the end of six months and of these the majority are in good clinical condition. The response is better in those over three years of age; and early diagnosis (even before complete bacteriological data are available), which means prompt treatment, leads to more favourable responses. Relapses are common, and residual neurological disorders—mental backwardness and behaviour changes—have been noted. Lincoln and her associates (1948) suggest that the combination of streptomycin and "promizole" gives greater benefit. Of seven patients so treated, six were alive at from three to eight months after the beginning of treatment; all were mentally normal and free from pronounced neurological damage.

In *acute hæmatogenous miliary tuberculosis* prompt treatment is necessary, but it must be remembered that several conditions may simulate the radiological appearances of miliary tuberculosis, e.g. sarcoidosis, miliary carcinomatosis, aspergillosis and other fungoid infections, pneumoconioses, periarteritis acuta nodosa, lymphadenoma, congestive cardiac failure, Læffler's syndrome, and neurofibromatosis.

Combined parenteral and local treatment is indicated in *discharging cutaneous sinuses* (provided an underlying abscess is drained), in *tuberculous laryngitis*, and in *ulcerating tuberculous lesions* of the oropharynx and the tracheo-bronchial tree (by aerosol inhalations). Further experience is needed, despite many satisfactory clinical records, to evaluate the rôle of streptomycin in tuberculosis of the genito-urinary tract, bones and joints, skin, lymph nodes, and eye.

The most promising results following treatment in *pulmonary tuberculosis* are found in recent though extensive and progressing lesions, especially if these are diffuse and finely disseminated in radiological appearance, rather than dense, large, localized shadows. Tuberculous pneumonia should also be treated with streptomycin, but it is not advised in (a) chronic fibroid or fibrocaseous pulmonary tuberculosis, (b) acute destructive and apparently terminal types, (c) chronic tuberculous empyema, and (d) pulmonary tuberculosis with a favourable prognosis from conventional therapeutic measures, because of the toxic effects of the drug and the dangers of drug-resistant bacilli developing. More extensive and more adequately controlled studies may well modify our present views on the possibilities and limitations of streptomycin therapy in pulmonary tuberculosis. With the examples of tuberculin and sanocrysin in mind, we must refrain from unbridled optimism, but the impressive results in tuberculous meningitis and miliary tuberculosis raise justifiable hopes. Two points remain for emphasis; first, streptomycin cannot remove the mechanical changes resulting from healing, e.g. bronchial or ureteric strictures following ulceration; and secondly, streptomycin cannot be regarded at this time as a satisfactory substitute for established therapeutic methods in pulmonary tuberculosis—sanatorium care, collapse therapy and surgery.

In non-tuberculous infections.—Recent reports indicate the drug's value in *granuloma inguinale* (Kupperman *et al.*, 1948) and in *rhinoscleroma* (Devine *et al.*, 1947). It is, however, in many gram-negative bacillary infections, in which penicillin fails and the response to sulphonamides is uncertain, that streptomycin has proved so valuable. It is effective in urinary tract infections, wound infections, and bacteraemia due to *Escherichia coli*, *B. proteus*, *Pseudomonas aeruginosa*, and *Aerobacter aerogenes*; in influenzal meningitis and pneumonia, in meningitis due to all forms of gram-negative bacilli, in infections due to *Klebsiella pneumoniae*, in plague, in Haverhill fever due to *Streptobacillus moniliformis*, in tularaemia, and in Shigella dysentery.

Dosage and administration.—The sensitivity of the infecting organism controls the precise dosage of streptomycin, but in general 2 to 3 gm. daily, by intramuscular or subcutaneous injection, in three to four divided doses should be given (although Feldman *et al.* [1947b] suggest that two doses are adequate); but in chronic infections, 1 to 2 gm. daily is usually sufficient to control the disease. The sulphate or hydrochloride may be dissolved in

sterile pyrogen-free water or in isotonic sodium chloride solution in a concentration of 100 to 500 mgm. per c.cm. The solution is reasonably stable if kept cold, but should be freshly prepared each day. Streptomycin is ineffective by mouth, and when injected intravenously may give undesirable side-effects. In meningeal infections, intrathecal injections of streptomycin are given daily or on alternate days, in a concentration of not more than 50 mgm. per c.cm., the full dose not exceeding 100 mgm. Severe meningeal and cerebral reactions have been observed, especially headache and somnolence approaching stupor. The two hazards of streptomycin therapy are its toxicity and the development of streptomycin resistance.

Toxic reactions.—Apart from local irritation at the site of injection, which is slight, and meningeal irritation from intrathecal injection, which may be marked, streptomycin may give four types of toxic reaction: (1) the so-called histamine reaction, characterized by flushing, headache, paraesthesiae of the hands, tongue, and circum-oral region, and an abrupt fall in arterial pressure; (2) various manifestations of anaphylaxis and allergy, similar to those seen, for example, after treatment with sulphonamides, thiouracil, and gold salts; (3) renal irritation with casts and red blood cells in the urine, and rarely anuria, especially in patients with previous renal damage; and (4) most frequent of all, impairment of function of the vestibular portion of the auditory nerve, as evidenced by vertigo, ataxic gait, and blurred vision (from impaired accommodation), though nystagmus is rare. The vestibular dysfunction appears about the twenty-first day of treatment, but complete symptomatic recovery occurs in practically all cases. Deafness and tinnitus are rare, although they may occur after intrathecal therapy. Hunnicutt *et al.* (1948) have reported a fatal toxic encephalopathy apparently caused by streptomycin, but the patient had both pyelonephritis and diabetes. In tuberculous meningo-encephalitis, the neurological disturbances which follow streptomycin therapy must be related to the disease as well as to the drug. Nursing personnel should avoid direct skin contact with streptomycin as this may cause a local dermatitis (Rauchwerger *et al.*, 1948).

Drug-resistance.—A serious handicap to prolonged and effective streptomycin therapy is the disappearance during treatment of drug-sensitive strains and their replacement by drug-resistant strains. This problem has been discussed earlier in its relation to penicillin, when the individual problem is, however, less grave because streptomycin resistance develops much more rapidly (in tuberculosis, drug-resistant bacteria may appear in appreciable numbers within sixty days of the institution of treatment); but larger initial dosage or the synergic combination of drugs (e.g., as in the use of streptomycin and "promizole" in tuberculous meningitis) may help to overcome this obstacle to effective therapy. In urinary tract infections, alkalization of the urine has proved a most valuable adjunct. At a pH of 8.0 the antibacterial effect of streptomycin is 80 times as great as at a pH

of 5.5; thus if the urine is kept alkaline between pH 7.5 and 8.0 a given dose is 80 times as effective as when the urine is kept acid between pH 5.5 and 6.0 (Harris *et al.*, 1947).

NEW ANTIBIOTICS

The literature of antibiotics continues to record a host of antibacterial substances derived from fungi (in their hundreds), actinomycetes and bacteria (Florey, 1947). Of these, three show therapeutic promise—polymyxin, aerosporin, and chloromycetin.

Polymyxin (Stansly *et al.*, 1947) is said to be five to ten times as effective as streptomycin in experimental infections in mice with *K. pneumoniae* and Pfeiffer's bacillus, and has been used clinically both in these and in undulant fever and pyocyaneus infections; but clinical trial is too limited for its just appraisal. Good results are claimed for *aerosporin* in pertussis (Swift, 1948).

Chloromycetin may prove to be of major importance. Reports from many sources confirm that it is effective against scrub typhus (tsutsugamuchi fever), the formidable foe of our troops in Burma. Laboratory experiment suggests that chloromycetin is equally effective against other rickettsial diseases. Should this hope to be translated into fact, a major scourge may be on the way to elimination.

This brief survey reveals the ever-expanding field of antibiotic endeavour. The limitations of the old, and the potentialities of the new and as yet unborn, are in clearer focus than they were a year ago. But the promise is unlimited, and patience, ingenuity and industry may yet provide antibiotics, natural and synthetic, which in future medical practice will relegate the infections from a major to a minor problem.

SPECIFIC THERAPEUTIC MEASURES IN INFECTIONS

Perrin Long (1947) emphasizes that when the physician is confronted with an infection which may respond to one of several chemotherapeutic or antibiotic agents, he should consider: (1) which agent will be most effective; (2) what is its relative toxicity; (3) the ease of administration; and (4) the cost and availability of the agent and its administration. He finds sulphadiazine less toxic than sulphapyridine, sulphanilamide and sulphathiazole, and states that sulphamerazine and sulphapyrazine appear to be somewhat less toxic than sulphadiazine. His views, with slight modifications and additions, on the choice of the appropriate agent for a large variety of infections are summarized on page 241.

ACUTE ANTERIOR POLIOMYELITIS IN 1947

By far the largest and most serious epidemic of acute anterior poliomyelitis which this country has experienced appeared in 1947. Many bizarre forms of the disease with cranial nerve involvement and clinical pictures of bulbar

AGENTS (BY ORAL OR PARENTAL ROUTES ONLY) FOR USE IN VARIOUS INFECTIONS.

(S=sulphonamide; Sg=sulphaguanidine, sulphasuxidine, or sulphaphthalidine;
P=penicillin; St=streptomycin).

(A). β -HÆMOLYTIC STREPTOCOCCUS

<i>Disease</i>	<i>Agent</i>
Tonsillitis	S ; P
Peritonsillar abscess	S ; P
Ludwig's angina	S and P
Acute sinusitis	S ; P
Otitis media	S ; P
Mastoiditis	S and P
Meningitis	S and P
Erysipelas	S ; P
Scarlet fever	S ; P
Adenitis	S ; P
Cellulitis	S ; P
Pneumonia	S and P
Empyema	S and P
Peritonitis	S and P
Puerperal sepsis	S and P
Osteomyelitis	S ; P
Ulcers	S ; P
Impetigo	S (P contraindicated)

(B). NON-HÆMOLYTIC OR α -STREPTOCOCCI; AND OTHER ORGANISMS

<i>Disease</i>	<i>Agent</i>
Subacute bacterial endocarditis	P
Pneumococcal infections	S ; P
Pneumonia	S ; P
Meningitis	S and P
Peritonitis	S and P
Otitis media	S and P
Mastoiditis	S and P
Sinusitis	S and P
Meningococcal infections	P
Gonococcal infections	S ; P
Staphylococcal infections	S ; P
<i>Escherichia coli</i> tissue infections	S ; St
Gas gangrene	S and P
Cholera	S
Tularæmia	St
Tuberculosis (selected cases)	St
Influenzal meningitis	S and St
Plague	S
Infections due to Friedländer bacillus	S and St
Bacillary dysentery	S and Sg
Brucellosis	S and St
Typhoid infections	S and P (?)
Salmonella infections	S and P
Chancroid	S
Urinary tract infections:	
<i>Aerobacter aerogenes</i>	S ; St
<i>Escherichia coli</i>	S ; St
<i>Pseudomonas aeruginosa</i>	S ; St
<i>Proteus vulgaris</i>	S ; St
Actinomycosis	S ; P
Anthrax	S ; St
Trachoma	S
Lymphopathia venereum	S
Ulcerative colitis	Sg (?)
Psittacosis	P
Influenza (secondary infections)	As for secondary infections
Common cold (secondary infections)	As for secondary infections
Rheumatic fever (prophylaxis only)	S
Syphilis	P
Yaws	P

(First agent mentioned is first choice; drugs not recommended are contraindicated.)

paralysis and transverse myelitis were recognized during the epidemic; indeed, few neurological syndromes escaped mimicry. The important part played by abortive or subclinical types in the spread of infection has been confirmed. Ritchie Russell's careful study (1947) of 44 patients strongly suggests that the extent of paralysis is related to the physical activity of the patient during the early phase of the infection. Those who retire to bed at the onset of symptoms escape most often the graver paralyses. Hence the importance of early diagnosis during the meningitic phase when radicular pains and resulting muscle spasms are so commonly found.

BLOOD DISEASES

Since Minot and Murphy, twenty-two years ago, postulated the presence in liver of a factor the absence of which led to *pernicious anæmia* and its neurological accompaniments, there have been many attempts at its isolation in pure state. The latest phase in the quest is recorded in two independent researches, one from Britain (Smith, 1948a) and one from the United States (Rickes *et al.*, 1948). Both groups isolated a red substance of extremely high potency.

In his latest note Smith (1948b) reports that the ash of his red crystals unexpectedly revealed the presence of cobalt in an amount suggesting that if each molecule of his crystalline material contains one atom of cobalt, its molecular weight would be about 1,500. The presence of cobalt is of interest as it is an essential trace element and has been shown to prevent and cure in ruminants an anæmia due to feeding on pastures deficient in cobalt (Martin, 1944).

The American substance, for which the name vitamin B₁₂ is suggested, is effective in a single dose of 15 µgm. or a daily dose of 1 µgm., which is roughly two thousand times more potent as a hæmopoietic agent than folic acid; but twenty tons of liver are needed to yield 1 gm. of crystals. It is claimed also that these red pigments are effective both in the prevention and therapy of the neurological accompaniments, but in view of the frequently delayed development of these it would be wise to reserve judgment on this until further evidence is forthcoming.

It is clear that folic acid has only a limited place in the treatment of anæmias and is inadequate alone for the routine treatment of pernicious anæmia, although it is an agent of value in the anæmias of steatorrhœa, nutritional deficiency states, and in certain other megaloblastic anæmias which are refractory to liver and are unassociated with changes in the nervous system.

A notable practical advance in the treatment of *iron-deficiency anæmias* was recorded by Nissim (1947) and later reports have confirmed his claims. He found that saccharated oxide of iron, a B.P.C. preparation containing about 3 per cent. of metallic iron in sucrose and forming a freely soluble reddish brown powder, could be given intravenously in 1 per cent. solution without significant toxic effects even when 500 mgm. in 50 c.cm. were

injected in seven minutes. It can be given in more dilute form as a 0.1 per cent. solution of saccharated iron oxide in 5 per cent. dextrose. A dose of 500 mgm. causes a rise of about 20 per cent. in hæmoglobin, which conforms to that which earlier work had led us to expect. Slack and Wilkinson (1948) have recorded the use of an intravenous iron-sucrose complex, similar to that used by Nissim, which had given satisfactory responses and was free from reactions in the day-to-day outpatient treatment of 55 cases of iron-deficiency anæmias. Using the proprietary preparation, "ferrivenin", I have found most gratifying response in patients who cannot tolerate iron by mouth.

In the *leukæmias* and *lymphomas*, including Hodgkin's disease, lymphosarcoma and mycosis fungoides (Osborne *et al.*, 1947), recent reports of treatment by newer methods, especially urethane, nitrogen mustards, and systemic irradiation with such radio-active isotopes as those of phosphorus, sodium, manganese and gold, have failed to substantiate earlier claims of their greater efficacy or their advantages over older methods of radio-therapy. All forms of treatment in this group remain palliative. Early diagnosis and wise judgment in the choice and application of available means of treatment will, however, improve the lot of the patient and postpone the as yet inevitably fatal outcome.

RADIO-ACTIVE ISOTOPES

No dramatic advances in the field of therapy with radio-active isotopes have recently been recorded. Lawrence *et al.* (1948) have published a study of 129 patients with chronic myelogenous leukæmia treated with radio-active phosphorus (P^{32}) alone or combined with X-rays, and find that a third are living or have lived for five years or more after the onset of symptoms. Studies which report beneficial results from radio-active iodine in thyrotoxicosis and post-thyroidectomy recurrences continue to appear, but in cancer of the thyroid this agent has not been generally effective. For polycythæmia, radio-active phosphorus appears to be the most valuable therapeutic agent now available, and certain types of neoplasm have been successfully treated by direct neutron bombardment. Attempts have been made to secure selective irradiation of the lymphatic and reticulo-endothelial systems by injecting colloidal solutions of radio-active isotopes of certain metals (most recently gold) which are deposited in these cells. Remissions have been produced in lymphatic leukæmia using these methods. Radio-active gold has also been infiltrated directly into tumour masses with, it is claimed, good results, but the observations recorded must not be looked upon as more than preliminary studies. Warnings have been issued (Muller, 1947) about the destructive effects on germ cells which may follow the use of radio-active isotopes, and the consequences to progeny, but in the treatment of fatal disease this is not a major consideration. The ease with which they can be recognized in tissues has led also to their diagnostic use; for

example, Rotblat and Ansell (unpublished work) have taken advantage of the special affinity of the thyroid for iodine to use radio-active iodine in the diagnosis of substernal goitre.

The most fruitful present use of isotopes is undoubtedly the aid they give as "tracers" in the study of fundamental biological processes in animals and man. In this form such elements as phosphorus, iron, sodium, carbon, and iodine can be traced in the body and their rôle in metabolism determined.

BRITISH ANTI-LEWISITE (BAL)

During the year further evidence has been forthcoming which confirms the value of BAL (2,3-dimercaptopropanol) in the treatment of metallic poisoning. An M.R.C. Committee (Peters *et al.*, 1947) reports that of 44 cases of *arsenical dermatitis* 31 benefited from treatment with BAL, 23 strikingly so, and that the mean duration from the onset to the cure of the dermatitis was twenty-one days. Eagle and Magnuson (1946) obtained similar good effects in dermatitis; in 11 patients with arsenical agranulocytosis 10 showed rapid clinical and hæmatological improvement. The results of treatment, however, in both toxic arsenical encephalopathies and in jaundice were uncertain.

In *poisoning due to swallowing mercuric chloride* (corrosive sublimate) BAL has proved its worth (Longcope and Luetscher, 1946). It should be borne in mind as a possible agent of value in the rare cases of poisoning which follow the use of mercurial diuretics.

There is also ample evidence that the *dermatitis and toxic blood complications of gold therapy* in rheumatoid arthritis yield to the administration of BAL (Ragan and Boots, 1947; Lockie *et al.*, 1947). In animals the toxic effects of other metals—nickel, cadmium, chromium and antimony—are antagonized by BAL, so that it is likely that cases of poisoning by these metals, a toxic hazard in industry, could be usefully treated by the drug. The dosage recommended varies with different authors, but it is effective when given by intramuscular injection in an initial dose of 0.3 gm. in 10 per cent. solution followed by 0.15 to 0.45 gm. in the ensuing twelve hours; depending upon the response, the total amount for a full course lasting three to four days should be 1 to 3 gm.

CONCLUSION

The foregoing survey touches only a few of the fields in which advances have recently been recorded. In special contributions to this number are described many other important measures, the permanence of whose place in our therapeutic armamentarium has yet to be determined. The invasion of surgery into cardiovascular disease is no longer confined to patent ductus arteriosus, coarctation of the aorta, Fallot's tetralogy, and essential hypertension. Portocaval shunts have become surgical realities in the treatment of portal hypertension. There has been a direct attack by Brock (1948) on

the stenosed pulmonary valve. He has designed a cardioscope carrying a guarded blade which will enable him to cut the valve under direct vision. The major obstacle to prolonged intracardiac surgery is the need to maintain the brain circulation during the operation. Anticoagulants, e.g. heparin, and mechanical hearts harnessed to the patient while his great vessels are occluded, may well solve the technical difficulties presented. There is here a fascinating prospect of cooperative achievement by the physician, surgeon and physiologist.

Peptic ulcers still present their mysteries, not wholly unmasked by psychosomatic phrases, or solved by vagotomy.

The value of *thiouracil in the treatment of thyrotoxicosis* has been established. The methyl and propyl forms are least toxic and can be used with safety in the ambulatory patient. White blood counts do not help to forestall toxic granulocytopenia, which is of sudden onset revealing itself by fever or sore throat, for which penicillin is indicated. There is still much controversy about the relative merits of thiouracil and thyroidectomy for uncomplicated thyrotoxicosis. Physicians naturally tend to the conservative in treatment, but most would agree that surgery is indicated in (1) large intrathoracic goitres; (2) goitres which are rapidly increasing in size, especially if irregularly nodular and hard; (3) non-cooperative patients; (4) if pressure symptoms are marked; (5) if the goitre is unsightly, and (6) if thiouracil proves toxic or fails to lower the basal metabolic rate.

The year has seen the introduction of a galaxy of antihistamine drugs, but many of these have yet to prove their value in allergic states; of more potent anticholinesterases in the treatment of myasthenia gravis; and of a host of other remedies. So far as we know, there has been no major discovery. "So far as we know". But who can tell? Let it not be forgotten that after Fleming published his great work on penicillin more than ten years were to pass before its full therapeutic import was realized. Perhaps to-day in a remote laboratory "some mute inglorious" Fleming is at work, and standing on the threshold,

"Th' applause of listening senates to command,
The threats of pain and ruin to despise".

References

- Barber, M. (1947): *Brit. med. J.*, **ii**, 863.
 Bevan, G., et al. (1948): *Lancet*, **i**, 546.
 Brock, R. C. (1948): *Brit. med. J.*, **i**, 1121.
 Dempsey, T. G. (1948): *Ibid.*, **ii**, 148.
 —, and Logg, M. H. (1947): *Lancet*, **ii**, 871.
 Devine, K. D., et al. (1947): *Proc. Mayo Clin.*, **22**, 585.
 Eagle, H., and Magnuson, I. (1946): *Amer. J. Syph.*, **30**, 420.
 Erdei, A., and Snell, W. E. (1948): *Lancet*, **i**, 791.
 Faget, G. H., et al. (1946): *Int. J. Leprosy*, **14**, 30.
 Feldman, W. H., et al. (1947a): *Proc. Mayo Clin.*, **22**, 473.
 —, et al. (1947b): *Amer. Rev. Tuberc.*, **56**, 346.

- Feldman, W. H., and Hinshaw, H. C. (1948): *Brit. med. J.*, **i**, 87.
 Florey, H. (1947): *J. Amer. med. Ass.*, **135**, 1047.
 Harris, H. W., et al. (1947): *Amer. J. Med.*, **2**, 229.
 Hart, P. D'Arcy (1946): *Brit. med. J.*, **ii**, 805, 849.
 Hunnicutt, T., et al. (1948): *J. Amer. med. Ass.*, **137**, 599.
 Kupperman, H. S., et al. (1948): *Ibid.*, **136**, 84.
 Lawrence, J. H., et al. (1948): *Ibid.*, **136**, 672.
 Lehmann, J. (1946): *Lancet*, **i**, 15.
 — (1948): *Brit. med. J.*, **ii**, 148.
 Lescher, F. G., and Richards, H. R. M. (1947): *Ibid.*, **ii**, 565.
 Lincoln, E. M., et al. (1948): *J. Amer. med. Ass.*, **136**, 593.
 Lockie, W., et al. (1947): *Ibid.*, **133**, 754.
 Loewe, L., et al. (1947): *Science*, **106**, 494.
 Long, P. H. (1947): *New Engl. J. Med.*, **237**, 837.
 Longcope, W. T., and Luetscher, J. A., Jun. (1946): *J. clin. Invest.*, **25**, 557.
 McDermott, W., et al. (1946): *Ibid.*, **25**, 190.
 McSweeney, C. J. (1946): *Lancet*, **ii**, 114.
 Martin, C. J. (1944): *Proc. Nutrit. Soc.*, **1**, 195.
 Martin, J. P. (1948): *Brit. med. J.*, **i**, 922.
 Miller, C. P., and Bohnhoff, M. (1945): *Presc. Soc. exp. Biol.*, N.Y., **60**, 356.
 Muller, H. J. (1947): *J. Hered.*, **38**, 259.
 Nissim, J. A. (1947): *Lancet*, **ii**, 49.
 Osborne, E. W., et al. (1947): *J. Amer. med. Ass.*, **135**, 1123.
 Parsons, C. G. (1948): *Lancet*, **i**, 510.
 Peters, R. A., et al. (1947): *Brit. med. J.*, **ii**, 520.
 Ragan, C., and Boots, R. H. (1947): *J. Amer. med. Ass.*, **133**, 752.
 Rauchwerger, S. M., et al. (1948): *Ibid.*, **136**, 614.
 Report of Streptomycin in Tuberculosis Trials Committee (M.R.C.) (1948): *Lancet*, **i**, 582.
 Rickes, E. L., et al. (1948): *Science*, **107**, 396.
 Russell, W. Ritchie (1947): *Brit. med. J.*, **ii**, 1023.
 Slack, H. G. B., and Wilkinson, J. F. (1948): *Ibid.*, **i**, 753.
 Smith, E. L. (1948a): *Nature*, **161**, 638.
 — (1948b): *Ibid.*, **162**, 144.
 Speiser, M., et al. (1947): *J. vener. Dis. Inform.*, **28**, 108.
 Stansly, P. G., et al. (1947): *Bull. Johns Hopk. Hosp.*, **81**, 4.
 Stewart, H. C., and May, J. R. (1947): *Lancet*, **ii**, 857.
 Swift, P. N. (1948): *Ibid.*, **i**, 133.
 Worster-Drought, C. (1947): *Brit. med. J.*, **ii**, 559.

ADVANCES IN SURGERY

BY IAN AIRD, CH.M., F.R.C.S.

*Professor of Surgery, University of London; Director, Department of Surgery,
Postgraduate Medical School, London.*

ADVANCES in surgical treatment during the past year have taken the form chiefly of development of operative procedure and assessment and reassessment of the results of operations recently introduced.

CANCER OF THE BREAST

Perhaps the most controversial subject in surgical therapeutics during the past year has been the treatment of cancer of the breast. Most argument centres round the Edinburgh experiment on breast cancer which has been carried out under the direction of Dr. Robert McWhirter. McWhirter has shown conclusively that in Edinburgh the results of treatment by local excision of the breast and postoperative irradiation over a period of five years have been better than a series treated previously by radical amputation and irradiation, and a still earlier series treated by radical amputation alone. In the removal of the breast which McWhirter advises, the pectoral muscles and fascia are not disturbed and the breast is removed together with the tumour and a relatively small area of skin. Irradiation begins a few days after healing of the wound. The arguments in favour of this management are the high proportion of five-year cures, the possibility of very early postoperative irradiation, and the almost complete elimination of local recurrence. Radical amputation of the breast still has its ardent advocates, notable among them being Sir Gordon Gordon-Taylor, whose personal experience has been unrivalled and whose cure rate is high by any standards, and Sir Stanford Cade, whose understanding of radiological technique is unique among surgeons of eminence.

Briefly the arguments raised against McWhirter are these :—

(1) The figures in the earlier series of cases treated by radical surgery and irradiation were smaller than in the later series treated by local surgery and radiotherapy; it is argued that successes from the radical operation may have been excluded from the earlier series.

(2) The operative mortality in the control series treated by radical excision was relatively high.

(3) To some extent McWhirter's figures depend upon the assumption that the ultimate survival rate can be predicted relatively early in the follow-up period by extrapolation of a statistical curve. Cade argues that the survival rate in untreated cancer of the breast is three years and that even a five-year survival rate is not a true test of cure.

(4) The results of radiotherapy, performed by a single and enthusiastic expert, are compared with the results of radical operation performed by approximately twenty separate surgeons, not all equally interested or equally experienced in breast surgery.

The weakness of the argument advanced by those in favour of radical surgery lies in their acceptance of local excision and radiotherapy as a suitable treatment for

stage 3 and perhaps also for stage 2 cancers of the breast with axillary gland involvement; McWhirter properly argues that if a method of treatment is acceptable for cancers of the breast which have spread to the axilla, it must also be suitable for those cases in which the axillary glands are not in fact diseased, and in which local operation alone might sometimes be expected to effect a cure.

The importance of an experiment of this kind can hardly be underestimated. In the meantime it would probably be true to say that, for their wives, most surgeons would prefer a stage 1 cancer of the breast to be treated by the radical operation in the hands of an expert, and by subsequent irradiation. For stage 3 cancer of the breast the same surgeon would probably prefer a local excision with early and intensive postoperative radiotherapy. In stage 2 cases, with invasion of the axillary glands alone, opinion is too diverse to guess its present trend.

The *hormone treatment* of carcinoma of the breast proceeds everywhere as the method of choice for advanced cases with skeletal metastases, and indeed for most cases of hopeless cancer of the breast or hopeless recurrence after treatment. In patients during the child-bearing period this treatment takes the form of radiological or surgical oöphorectomy followed by the administration of testosterone in large doses. The common dosage level is 200 mgm. per day. This cannot be given without side-effects which are always unpleasant and sometimes serious: hirsuties of male type is inevitable, and sometimes a serious oliguria may threaten the function of the kidneys. For patients who have passed the menopause stilbæstrol therapy continues to be the most effective method of treatment.

PEPTIC ULCERATION

The studies of Orr and Johnson (1947) at the Postgraduate Medical School, of Beattie (1948) at Leicester, and of others, show that the early promise of *vagotomy* is likely to be maintained. Vagotomy may now be regarded as a satisfactory and safe method of treatment for duodenal ulcer in patients who have a high secretion of acid during the night hours and in response to insulin. The operation is valueless unless the night secretion and insulin response are abolished after it. It should not be performed as the sole method of surgical treatment if there is any pyloric stenosis. The patient who requires operation for the treatment of acute hæmorrhage should have a gastrectomy done. It is doubtful whether vagotomy is desirable in patients in the older age-period, but it has not yet been proved unsuitable for these cases.

Vagotomy has no serious after-effects if performed in suitable cases. There is some failure of the stomach to empty satisfactorily during the early postoperative period, but gastric contraction is quickly regained if the stomach is kept empty by suction for a few days after operation. Intestinal distention is not disturbing. A more serious effect of vagotomy, due either to direct damage to the œsophagus or to reflux of gastric contents into it, is the dysphagia which occurs in 2 or 3 per cent. of cases and which is sometimes apparently due to an acute ulcer of the lower œsophagus; patients so

affected recover within a few weeks. The most satisfactory feature of vagotomy is the apparently complete safety of the operation. Long-term results are still not available, but in more than one hundred cases operated on by Orr there has been no perforation and only one case of hæmorrhage in patients who have now lived for periods up to three years after vagotomy. The patient who bled was known, before his perforation occurred, to have had an incomplete vagotomy.

Vagotomy abolishes the psychic secretion of gastric juice; it has no effect on the hormonal secretion which occurs in response to food. To abolish gastric acidity completely, to give a complete guarantee against recurrence of hyperacidity, and to permit an operation to be applied even to cases of pyloric stenosis, vagotomy must be combined with excision of the antrum of the stomach. This entails a limited gastrectomy which must have a low mortality in comparison with the extensive gastrectomies generally advised for ulcer. It is true that in the past, gastrectomy for peptic ulcer has had, in the best hands, a mortality of 2 per cent. or less; it is impossible to say what the mortality of gastrectomy is over the whole country, but it would be fair to compute it to be between 5 and 10 per cent.; any effective alternative procedure with a mortality of one per cent. or less would be welcome.

Vagotomy still remains an operation for the research centre, but it is likely very shortly to be sufficiently standardized for general adoption. It has proved necessary to say, as has so often been said before, that vagotomy is useless in the treatment of gastric ulcer.

CARCINOMA OF THE COLON

The more insoluble drugs of the sulphonamide series have now made colectomy a relatively simple procedure, and have nearly, but not quite, abolished the need for a preliminary defunctioning colostomy, except in the case of patients who have acute obstruction when first seen.

Conservative resection of the rectosigmoid is becoming rapidly more general, although many experienced authorities deplore the tendency to extend the conservative technique downwards into the rectum. There is no question, however, that patients who suffer from carcinoma of the rectosigmoid or of the very uppermost peritonealized stretch of rectum can now be spared the inconvenience and indignity of a permanent colostomy.

The technique most generally employed is an anterior resection with or without temporary transverse colostomy. The abdomen is opened and the rectum thoroughly mobilized from above; the tumour is resected, and end-to-end anastomosis is established between pelvic colon and lower rectum.

MEGACOLON

Telford and Haxton (1948) have recorded a most satisfactory series of cases of megacolon treated by the method of lumbar puncture, repeated if necessary, first introduced by Margaret Hawksley. The rationale of this procedure depends upon the interruption of sympathetic pathways, thus

leaving the parasympathetic evacuant nerves in full functional control of the colon. The same arguments may be raised in connexion with this management of the disease as were used to explain the failure of sympathectomy to affect the size of the colon at all, or even to improve the function of the colon permanently. A period of some weeks in hospital with adequate emptying of the bowel by vigorous enemas, particularly if enema administration is continued after the patient leaves hospital, is very successful in relieving the obstipation temporarily, even without intervention upon the sympathetic system by operation or by spinal anæsthesia. In many centres of children's surgery recurrence of symptoms after sympathectomy and lumbar puncture has been so universal that there is already a trend towards more radical surgery. By modern methods a complete colectomy can be done safely in stages.

I have performed one successfully on a child of eleven months who had suffered, while a month old, from acute obstruction due to megacolon treated by colostomy; this child failed to respond to repeated spinal anæsthesia and to sympathectomy.

TRANSPLANTATION OF URETERS

The mortality rate of transplantation of the ureters for extraversion of the bladder has always been relatively low, but the postoperative mortality of the same operation performed as a preliminary stage before resection of the malignant bladder has in the past been exceedingly high. The modern extraperitoneal technique is substantially safer.

The operation is done on the left side first, the ureter being approached extraperitoneally. A small opening is made in the peritoneum through which the pelvic colon may be delivered, but after its delivery the edges of the opening in the peritoneum are sutured to the bowel before the ureter is implanted in it. The technique of implantation is of the simplest, the ureter being laid in a groove in the colon and made to protrude a little, as a nipple, into the lumen. A few weeks later the operation is done on the right side, the right ureter being implanted in the region of the pelvic-rectal junction.

HYPERTENSION

Whilst it is most unlikely that sympathectomy of any kind will prove the final answer to the treatment of hypertension, there is certainly no procedure available now which can offer the same prospect of alleviation to the hypertensive patient.

At the July meeting of the British Medical Association at Cambridge this year Smithwick (1948) read a paper on surgery in hypertension before the joint sections of Medicine and Surgery. The paper comprised a review of 256 cases followed for five to nine years and must be regarded as the most authoritative consideration of the subject.

Smithwick continues to advise the thoraco-lumbar operation which provides for an adequate sympathectomy together with inspection and biopsy of the kidneys and examination of the adrenals—an adrenal tumour causes sustained rather than intermittent hypertension in some 5 per cent. of cases.

Smithwick performs the operation in two stages, the second side some ten days after the first, and his mortality rate is in the region of 10 per cent. Thirty-one per cent. of all his patients died five to nine years after operation. The effects of the operation upon the various vascular areas in the survivors was estimated by three criteria:—

(1) Retinal changes were improved in 40 per cent. and worse in 20 per cent.
(2) Cardiac function, as measured by electrocardiogram, was improved in 42 per cent. and worse in 9 per cent.

(3) Renal function was improved in 29 per cent. and was worse in 10 per cent. The diastolic pressure fell to, and remained at, 90 mm. Hg in 35 per cent. of cases for a period of five years, and in 21 per cent. of cases for a period of nine years. The diastolic pressure fell to less than 110 mm. Hg and remained there in 42 per cent. of cases for five years and in 33 per cent. for nine years. In fact, only half of the patients who seemed to be improved during the first five years after operation maintained that improvement during the second period of five years.

Subsequent discussion at the same meeting showed clearly that the eye changes after operation were sometimes quite remarkable.

The operation is performed both in benign and in malignant hypertension, but a blood urea of over 100 mgm. per cent. is a contraindication, as also is cardiac asthma. Early renal damage is no contraindication. In this country there is a trend towards still more extensive sympathectomies. Smithwick restricts his operation to a removal of the lumbar chain between the eighth thoracic and first lumbar segments, but with the use of a transpleural approach English operators are now resecting the chain as high as the third thoracic ganglion, although this may be followed by severe postural hypotension and tachycardia.

These sympathetic operations reveal a greater number than might be expected of adrenaline-producing tumours of the adrenal gland. As Smithwick has pointed out, such a tumour may be suspected if there is (a) a severe fall in the high blood pressure when the patient assumes the erect position; (b) pronounced tachycardia; (c) a high basal metabolic rate, unusual muscle twitching, or pyrexia. A useful test for the presence of a tumour of this kind is the fall in the blood pressure which follows injection of histamine, but intravenous histamine injection in these patients is not without danger, and it would seem wiser to have recourse to the new adrenalytic agents, D.H.K., and benzodioxane, for this diagnostic purpose.

CONGENITAL ATRESIA OF THE ŒSOPHAGUS

Franklin (1948) in this country has now added to the successful number of operations for congenital Œsophageal atresia that have been reported from the United States. Franklin's three successes, the first to be recorded in this country, show the importance of the early recognition of this condition, and of the avoidance of indiscriminate barium swallow in these unhappy infants.

In most cases the Œsophageal obstruction is near the bifurcation of the trachea, and the lower Œsophageal segment usually communicates with the trachea by fistula, so that unless operation is performed early, gastric con-

tents regurgitate into the trachea from the lower segment, and the upper segment overflows into the larynx, so that severe pulmonary infection is established early. The condition is suspected if the child returns the first feed, and diagnosis is confirmed by X-rays after the introduction of a little lipiodol into the proximal œsophagus by pipette. Operation is best performed on the second day after birth.

The right chest is explored by way of a mediastinal dissection without opening the pleural cavity. The fistula with the trachea is clamped and divided, and the tracheal opening is closed. An opening is then made in the proximal segment of the œsophagus which is anastomosed to the distal segment.

CARCINOMA OF THE ŒSOPHAGUS AND CARDIA

The early surgical researches of Ohsawa, Garloch and Phemister abroad, and those of Grey Turner and Franklin, Brock, Allison, Steele, Thompson and Lewis in this country, have made of excision of the œsophagus a standard surgical procedure. Indeed, so routine has the transpleural approach to the œsophagus become that it is now convenient to perform total gastrectomy by a modification of this route. It might be said to be standard to-day for transthoracic gastrectomy to be performed for extensive malignant disease (notably leather-bottle stomach) or for carcinoma of the cardia.

A transverse abdominal incision is first made across the rectus abdominus midway between umbilicus and xiphoid cartilage, for exploration of the abdomen and mobilization of the distal stomach, and that incision is then continued over the costal margin and along one of the lower intercostal spaces to open the left pleural cavity. The diaphragm is divided and the stomach, very often together with the spleen and the tail of the pancreas, is mobilized in its upper part and removed after division of the lower œsophagus. A loop of jejunum is then brought up and fixed to the mediastinal structures for the lower open end of the œsophagus to be implanted in it.

When the operation is performed for tumour of the cardia the distal stomach may be brought up into the chest in the same way for this anastomosis.

RESECTION OF THE LUNG

For long, lobectomy remained the treatment of choice in cases of bronchiectasis, but it is now recognized that bronchiectasis affects the lung not in lobes but in broncho-pulmonary segments—the anatomical unit of the lung corresponds, as does the bronchiectatic unit, to the portion of lung served by the bronchus and its related vessels. Brock has made a detailed anatomical study of these lung segments, and by radiological methods it is now possible to outline before operation which segments of which lobes are diseased, and it is possible at operation to remove the diseased segments, sometimes of multiple lobes, while leaving uninfected portions of lobes as functional lung units. Pilcher and others have shown that large fractions of the total volume of pulmonary tissue may be removed by segmental resection, particularly in children suffering from bronchiectasis. Pilcher (1946) has removed, from a child of twelve, both middle lobes, the lingula,

one lower lobe and segments of the remaining lower lobe and of both upper lobes, to leave the child with an adequate vital capacity.

In the modern operation of segmental resection the bronchial division of the segment under attack is exposed first and ligated. The segment of lung served by the ligated bronchus collapses and its demarcation from adjacent segments is at once obvious if the general intrabronchial pressure is raised.

Lobectomy and pneumonectomy have been performed by many surgeons for the treatment of tuberculous cavities, the closure of which by collapse methods has been found unsuccessful, or their resistance to collapse has been predicted. The fatality rate of lobectomy is still fairly high (7-15 per cent.) and that of pneumonectomy still higher (20-28 per cent.) (Sweet, 1946; Overholt *et al.*, 1946), and the many complications to be feared include tuberculous wound infection, empyema, fistula, spread of tuberculous disease to healthy lung, ulceration of the bronchial stump, pulmonary embolism, cardiac arrest and pulmonary œdema. Yet the tension cavity still remains the most serious problem in the surgery of pulmonary tuberculosis, and the risks of resection for this particular type of tuberculosis, and for lungs destroyed and functionless but still widely excavated by large cavities, have been shown perhaps to be justified. Massive hæmoptysis shown definitely to proceed from a cavity which has persisted after thoracoplasty is regarded as a specific indication for resection. Overholt and Sweet both record that approximately half of their cases chosen for resection were symptom-free and sputum-negative for a substantial period after operation. Overholt has performed more than 200 resections of lung for pulmonary tuberculosis.

TOXIC GOITRE

The treatment of toxic goitre has this year proved almost as controversial a subject as the treatment of carcinoma of the breast. The strongest case for surgical intervention was advanced by Geoffrey Keynes at a meeting of the Royal Society of Medicine last winter; the strongest argument for routine medical treatment was presented by Himsworth (1948) at the British Medical Association meeting at Cambridge this summer. Regarded from the point of view of the surgeon, thyroidectomy has many advantages. It returns the busy housewife to full duty within a few weeks, whereas thiouracil treatment requires a continued administration of the drug over a period of one, two, or more years. The mortality rate of operation is of the order of 0.5 per cent. in the best hands, perhaps 2 per cent. over the country as a whole; the mortality rate of thiouracil treatment is of the order of 0.5 per cent. Relapse after thiouracil treatment is rather more common than after surgery, and thiouracil gives disappearance of the swelling of the neck in only 10 per cent. of cases. Most of the patients, given a choice either by the surgeon or the physician, tend to choose surgery because of the rapidity of the cure which it effects and because of its guarantee of

removing the swelling in the neck. There is certainly now no more satisfactory operation in surgery than thyroidectomy performed for a patient with toxic goitre who has been prepared by thiouracil.

There are certain disadvantages in thiouracil therapy which have not, so far as I know, been advanced elsewhere but which seem to me to be important. Formerly patients suffering from toxic goitre with auricular fibrillation did not commonly develop a peripheral arterial embolism when the auricular fibrillation was brought under control, presumably because the rapid circulation rate prevented formation of a clot within the auricle during fibrillation. Since the introduction of thiouracil I have seen several instances of peripheral arterial embolism, some of them severe, and presumably due to the formation of clot in the auricle, which continues to fibrillate for a time after the basal metabolic rate and the circulation rate are slowed; so that when, subsequently, the auricular fibrillation too comes under control, fragments of clot are dislodged. It would seem desirable still to bring auricular fibrillation under control first by quinidine, or perhaps even by operation, rather than to correct the metabolic acceleration of toxic goitre too rapidly and before cessation of fibrillation.

A second practical disadvantage of the introduction of thiouracil has been the delay in diagnosis of certain non-toxic conditions affecting the thyroid gland. Patients with goitrous swellings, sometimes wrongly considered to be associated with a mild degree of toxicity, seem now to be treated initially, and sometimes persistently, by thiouracil, and forms of thyroid enlargement which are in fact not amenable to thiouracil are nowadays sometimes slow in coming to the surgeon.

The early fear that the increased vascularity and size of a thiouracil-treated goitre made operation more difficult has not been substantiated. Sometimes the gland is very large and its venous connexions with the internal jugular vein extremely short, so that venous bleeding may be dangerous, but with adequate care there is no real danger to life and the patient prepared for operation by thiouracil and iodine withstands hæmorrhage much better than did those formerly prepared by iodine alone. The risk of myxœdema after thyroidectomy performed in a thiouracil-prepared patient is substantial, and I have observed it well established within three months of operation. It would seem wise, perhaps, to perform a rather less radical thyroidectomy in toxic patients who have been treated with thiouracil.

INTRATRACHEAL GOITRE

An interesting form of thyroid enlargement has been described within the last year by Lars Thoren (1947). He has collected some 80 cases of intratracheal and intralaryngeal goitres occurring as a projection of thyroid tissue within the lumen of the trachea or larynx in a patient with simple goitre. The protrusion takes the form of a sessile tumour, like half a cherry, covered by normal mucosa and lying at any level between the glottis and

the bifurcation of the trachea, usually in the upper trachea and on its left posterior aspect. Colloid, toxic, and malignant types have been described, but the first is by far the most common. It is uncertain whether this peculiar goitre is an enlargement of ectopic thyroid tissue, or a protrusion of extratracheal goitre through a congenital weakness in the tracheal wall. Oddly enough, the condition is more common in men than in women; it has been described at all ages. It gives rise to dyspnoea, cough or irritation, usually beginning at puberty, and in women most severe just before menstruation or in pregnancy. The condition should be particularly suspected if respiratory obstruction continues or increases after removal of a goitre. X-ray of the trachea may show a smooth, rounded endotracheal tumour. Treatment must be varied to suit the individual case.

If the extratracheal thyroid gland is goitrous, as it usually is, it is probably wise to divide the thyroid isthmus, and to perform tracheotomy below the level of the tumour as the first stage of operation. The trachea is then packed below the aberrant tissue and that tissue is removed before the operator proceeds to deal surgically with the extratracheal goitre.

SPLENECTOMY IN HÆMOLYTIC JAUNDICE

The work of Loutit and Mollison (1946) on the etiology of hæmolytic jaundice has not yet been generally applied by surgeons. These authors showed that, in the congenital type of the disease (Chauffard-Minkowski), there is a congenital defect in the red cells of the patient which, when transfused into a normal individual, undergo lysis; normal red cells transfused into a patient survive, and transfusion before, during, and after splenectomy in this congenital form of the disease may be almost light-heartedly undertaken provided donor and recipient are of the same group. In acquired hæmolytic jaundice, blood transfusion must be performed with great caution. This form of the disease is due primarily, not to abnormal fragility of the red cells, but to the presence of an abnormal hæmolysin; the cells of the blood transfused to the patient therefore undergo hæmolysis in spite of identity of blood group, and liberal transfusion may be followed by profuse hæmoglobinuria and sometimes by blockage of the renal tubules with pigment casts.

References

- Beattie, J. (1948): "Hunterian Lecture", R.C.S.
 Franklin, R. H. (1948): *Ann. Roy. Col. Surg.*, 2, 69.
 Himsworth, H. P. (1948): *Brit. med. J.*, ii, 61.
 Loutit, J. F., and Mollison, P. L. (1946): *J. Path. Bact.*, 58, 711.
 Orr, I. M., and Johnson, H. D. (1947): *Lancet*, ii, 84.
 Overholt, R. O., et al. (1946): *J. thorac. Surg.*, 15, 384.
 Pilcher, R. (1946): *Lancet*, i, 843.
 Smithwick, R. H. (1948): *Brit. med. J.*, ii, 237.
 Sweet, R. H. (1946): *J. thorac. Surg.*, 15, 373.
 Telford, E. D., and Haxton, H. A. (1948): *Brit. med. J.*, i, 827.
 Thoren, L. (1947): *Acta. chir. Scand.*, 95, 495.

ADVANCES IN OBSTETRICS AND GYNÆCOLOGY

By JAMES WYATT, M.B., F.R.C.S., F.R.C.O.G.

Consulting Obstetric Physician, St. Thomas's Hospital.

IN recording advances in treatment it is necessary to study carefully the results in a considerable number of cases and over a period of time, otherwise fallacious reports tend to arise.

The two recent outstanding discoveries, neither of which can be claimed by the obstetrician or the gynæcologist, but only their application, are: (1) that of the hæmatologist—the Rh factor; (2) that of the bacteriologist—penicillin.

THE Rh FACTOR

Obstetricians especially, will remember the disturbing factors of hydrops foetalis, of cases of death *in utero* shortly before term, and of cases of icterus gravis: they were labelled erythroblastosis, but the cause was unknown. Most unhappily, too, it was not fully realized that once established, unless a fresh mating took place, and then with the blood groups alike, the condition was almost bound to recur; and some poor woman wasted perhaps years in repeated pregnancies always hoping for a child who would survive.

The discovery of the Rh factor by Landsteiner and Weiner opened up a field in obstetrics for much research, and to-day this is being carried out all over the world, and already some of the myths that it might be responsible for repeated abortions and toxæmias have been exploded, but there is still much to be learnt.

To-day it is not possible to predict with certainty the result of the mating of an Rh- woman with an Rh+ man, even if the latter be homozygous; in fact an Rh+ mother may produce antibodies harmful to her foetus. There is no doubt, however, that the danger that exists of transfusing an Rh- woman with Rh+ blood is a real one, especially at a time when there is rather an over-enthusiasm for transfusion. Many patients have blood poured into them unnecessarily; in a few cases harmful to the recipient, and in others wasteful of the material. It is essential that if a transfusion has to be given to a woman, either before or during her child-bearing period of life, Rh- blood should be used if her Rh factor is unknown; then if she is a negative and her mate, or mate to be, a positive, she may at least produce one healthy child. I have little doubt that the time is not far distant when every female will have her Rh factor ascertained in early life; a small scar will then be made on her arm or leg denoting whether she is negative or positive and by this means some tragedies will be avoided. As Jenner's admirable work has for the time being been discarded, this mark may not be looked upon amiss.

With regard to *treatment*, this it is hoped will advance as knowledge of the whole subject becomes wider. As it is known that a number of healthy children can be borne by Rh- women of Rh+ men, interference with the pregnancy or active treatment of the new-born infant is unnecessary in the absence of further signs. It is also known that nothing can be done to prevent hydrops foetalis. Between these two we have the late death of the foetus *in utero*, which can sometimes be forestalled by induction of premature labour or by Cæsarean section.

A careful watch should be kept on the titre of the antibody in the mother, and if in the latter weeks there is a marked rise and then perhaps a fall, suggesting that it is being taken up by the foetus, termination of the pregnancy may save its life. Likewise after the confinement careful watch must be kept on the infant, and owing to the tendency to hæmorrhage it may be well that the mother be boosted with vitamin K shortly before delivery takes place. Blood examination should be carried out, and any sign of anæmia or jaundice must be met by transfusion with Rh- blood, and again it is advised that the donor be given vitamin K before the blood is taken.

Summing up, it seems essential that the Rh factor of every pregnant woman should be ascertained: if found to be negative then the husband should be investigated, and unless he is of a similar type the confinement should take place in hospital where special treatment both for the mother and her baby is available if required.

PENICILLIN

Puerperal infection.—The sulphonamides are an example of the importance of giving some time in the trial of a new preparation before assessing its full value. In the early days there was an inclination to believe that even the gross infections in the puerperium could be cured by the sulphonamides, but after extended trial it became evident that their main value was prophylactic; once a septicæmia or a general peritonitis was established they were seldom successful. Consequently the advent of penicillin was welcomed by those who had to deal with gross puerperal infections.

Perhaps it may be well to state here, however, that the organisms which infect the genital tract after abortion or childbirth are the same as produce infection in any other part of the body. For years the poor unfortunate woman so infected was almost looked upon as a leper, the only place that would accept her was the poor law infirmary, until in 1925 the Metropolitan Asylums Board opened a special unit for these cases, later carried on by the L.C.C. Surely the time has now come, with the advent of these new specific drugs, for all cases of serious infection to be treated in one unit. Special features would be necessary in the shape of a bacteriological service, a call on specialists according to the site of the main and subsidiary lesions, a medical officer-in-charge who is versed in chemotherapy, some form of bed isolation with, if possible, balcony facilities to nurse the patients in the open air when the weather allows, and last, but not least, efficient nursing

As regards the actual use of penicillin, if the patient obviously has a gross infection, treatment must be started at once; delay while a culture is being obtained may allow the organisms so to damage the tissues that even if a few days later the organisms have been destroyed by the drug, it is too late. Directly the bacteriological picture is obtained, and *it must be*, then if the organism is insensitive, it is no use subjecting the patient to the discomfort of further injections, and other lines of treatment should at once be carried out.

Dosage.—Already experience has shown that better results are obtained when a considerably higher dosage than that given in the early days of the drug are used. The earlier dosage of from 15,000 to 20,000 units three-hourly has been superseded in most cases by, in the early stages, 100,000 units three-hourly, and if the organism is resistant larger doses still will be necessary.

During treatment it is important to repeat the blood cultures and not to rely solely on the pulse and temperature, as in puerperal infections it is quite common to have a *B. coli* infection of the urinary tract. Bearing this in mind it is necessary for the urine to be examined bacteriologically and if a *B. coli* infection is found it should be appropriately treated. The length of time that the penicillin should be continued and the dosage must depend upon the findings in each case, but it is important not to stop this treatment too early, otherwise the infection may relapse. This should be borne in mind particularly in dealing with hæmolytic streptococcal infections other than Group A. When Groups B and C are found there is especial need to keep a careful watch on the heart; these organisms seem to have an affinity for endothelial cells and endocarditis is not uncommon. Also when the organism is resistant it may take much longer and with a much larger dosage of the drug to obtain first control and then cure, and up to 80 million units may be necessary.

One of the problems when this prolonged treatment has to be carried out is the discomfort caused by the injections; this does seem to vary but is very distressing to some patients. It seems to depend partly upon the method of injection, but is more likely due to the drug itself and is thought to depend upon impurities. Anyhow these are certainly less than they were in the early days, and this makes it hopeful that the solution of the difficulty is not impossible.

The anaerobic streptococci are not always easy to isolate, being slow in growth, and some days may elapse before a positive culture can be obtained. As their sensitivity varies it is important that treatment be started early, and it may here be necessary to continue for perhaps days before the offending organism is known. The clinical sign of repeated rigors would suggest an anaerobic infection, especially if arising in a case in which there had been retention of placental tissue which had to be manually removed.

Acute mastitis occurring in the lactating breast is, in over 90 per cent. of cases, due to the staphylococcus aureus, as a rule one of the most sensitive

organisms to penicillin. Much has already been done to relieve this condition if caught early, by complete cessation of suckling and the giving of large doses of stilboestrol to stop lactation. With treatment many cases are aborted; this number will be increased with the combination of two or three large doses of penicillin (250,000 to 500,000 units). What is particularly encouraging in this treatment is that, provided five to seven days' complete rest is given to the breast following the abatement of the lesion, it may be possible to get lactation completely re-established by again suckling the baby.

Prophylactically, penicillin powder alone or combined with a sulphonamide has been used with apparent success in those cases in which Cæsarean section has to be carried out after the patient has been in labour for some long time, or in which vaginal interference has taken place; it is usually powdered into the wound first after the lower segment of the uterus has been closed and again after the peritoneal flap has been sutured.

In gynæcology, penicillin has not had much application, except in acute salpingitis which commonly follows either an infected abortion or gonorrhœa. In both conditions spread of the infection to the Fallopian tube is often prevented by early treatment with chemotherapeutic measures. Should it occur, however, then, according to the infective organism, penicillin alone or in combination with one of the sulphonamides, provided suppuration has not already occurred, may abort the attack, even in some cases leaving the tube still patent. That this treatment has had a marked success is evident in any large gynæcological department by the rarity of the chronic pyosalpinx which is the exception rather than the rule nowadays.

STRESS INCONTINENCE

Many local operations on the fascia around the urethra and at the base of the bladder have been devised in attempts to relieve this unfortunate condition.

In those cases following childbirth a high percentage were successful but some failed, and to these may be added those in which the loss of control seemed to be of congenital origin, when the operative results were very poor. Some years ago on the continent, use was made of the fascia covering the abdominal muscles, strips of this fascia being brought down behind the symphysis pubis and fastened round the urethral neck.

In recent times this operation or a modification of it has been adopted in this country, the idea being that when the patient coughs or strains the abdominal muscles are active; this automatically tightens the fascia and the urethra is thereby closed and urine prevented from escaping. Millin and Chassar Moir recently reported to the obstetrical section of the Royal Society of Medicine on a number of cases in which success had followed failure after local operations.

It is not suggested that every case of stress incontinence should be so treated, when the more simple local operation is in so many cases successful, but it is certainly worthy of trial in the unsuccessful ones. Time alone will prove whether this fascial band will stretch or weaken as the tissues

so frequently do in advanced age, but in any event this operation may be the means of giving the patient some or many years of relief.

THE NEW HEALTH SERVICE

It was hoped that it might be embodied in the Act that the maternity services of the country should come under the direction of one authority. Unfortunately, the Government thought otherwise, and to-day, a woman who has her baby at home is under the jurisdiction of the local health authority, and the woman who has her baby in hospital, under the Regional Board, with, at present, no direct link.

It is well to remember that childbearing is a natural function, but from time to time, Nature fails, and it is important that this failure should be recognized early, and every attempt made to remedy it. This can only be done if all taking part in the Maternity Service have a close liaison, i.e., first that the midwife (who in the past, has been responsible for the greater part of this work) has ready access to an experienced practitioner, and that the practitioner, and those practitioners who are themselves carrying out this work, can readily obtain specialist help and access to hospital accommodation during pregnancy, labour and the puerperium whenever necessary.

One Regional Board is advising its Hospital Management Committees to set up at its key Obstetric Centre, a committee on which would serve the director of the department and his deputy, the medical officer of health, and representatives of those practitioners who themselves carry out maternity work, those who act for midwives, and a representative of the midwives and of the health visitors. This committee it is hoped, in the early days, will meet often, until the Service is established. By this means, the difficulties that tend to arise may be met and overcome. The midwives will be encouraged to seek help early, if any difficulty appears on the horizon, likewise the practitioners, and the latter should be encouraged to follow their cases in to hospital in order to see the treatment through.

One point of especial interest to-day, is the question of *analgesia and anæsthesia* during labour; this is not the time or place to discuss its pros and cons—it is being asked for, and should be provided, but this is not quite as simple as it seems. Every patient differs, first in the activity of the uterine action, and thereby in the length of the labour, secondly in what may be called her resistance to pain, and lastly, in the amount of drug that is necessary to overcome that pain. So far we have not achieved the perfect substance that will do its work without interfering with the uterine action, and injudicious use of both analgesics and anæsthetics may mean that a labour that would normally end naturally, has to be terminated artificially, with perhaps detriment to the mother or baby. It is only by a sound knowledge of the make-up of the patient, and a careful application of the analgesic or anæsthetic, that a happy result may be attained.

ADVANCES IN PÆDIATRICS

By A. V. NEALE, M.D., F.R.C.P.

Professor of Child Health, University of Bristol.

THERAPEUTICS within the age-groups of infancy and childhood continue to advance on a steady front. Notable progress has occurred in regard to meningitis, gastro-enteritis, prematurity, coeliac disease, and the surgical success in congenital heart disease, bronchiectasis, and abnormalities of the œsophagus and upper alimentary tract. The skilful handling of body fluid requirements and acid-base balance, and the appreciation of protein requirements in visceral defence, especially by the liver, combined with an increasing exactitude in the use of antibiotics and the sulphonamides, have all contributed. The subject is extensive and space will only allow a brief review.

PREMATURITY

Improved efficiency in the management of the premature baby has contributed to the new low record infant mortality rate. Good results can be achieved at home provided a skilful nurse is available, but very small babies are preferably treated in special premature units where room temperature and humidity are specially regulated and where œsophageal feeding methods are available. Breast milk is most valuable; the protein content can be strengthened in suitable cases. Recent experimental work (Gordon and Levine, 1947) has shown that the heavier premature baby soon acquires an ability for digesting cow's milk preparations. Vitamin K should be given immediately after birth. A rigid aseptic technique is fundamental. Efficient transport facilities must be available in each area; a premature baby may quickly succumb after a bad journey (Crosse, 1945). Facilities for oxygen should be available, as cerebral damage may arise in a short time from anoxia.

INFANT FEEDING

Breast feeding provides the *optimal* materials for *optimal* growth (*Brit. med. Bull.*, 1947), and it is almost axiomatic that human milk is never unsuitable. The protein is specially enriched by a high selective content of amino-acids and lactalbumen. Breast milk banks are proving of great value in providing supplies for debilitated or infected babies. If necessary, the protein content of breast milk can be increased by adding enzyme digests of casein. Waller (1946) has clearly outlined the causes and prevention of failing breast secretion: his methods are of outstanding importance and should be fully understood by all medical practitioners.

In the high protein feeding of wasted babies "casydrol oral with carbohydrate" (46 per cent. amino-acids and 43 per cent. lactol), or sodium caseinate (soluble protein) for babies over three months, may be used as

a 2 per cent. supplement to a standard feed. In the re-establishment of nitrogen balance 94 per cent. of the retained protein in hydrolysate is utilized for rapid replenishment of tissue protein.

Examples.—(1)

Breast milk	7½ oz. (233.3 gm.)
Water	2½ oz. (77.8 gm.)
Sugar	150 grains (9.7 gm.)
Casein hydrolysate.....	120 grains (7.8 gm.)
Protein	3.4 per cent.
Carbohydrate	9.0 per cent.
Fat	2.5 per cent.
20 calories per oz.	

(2)

Evaporated milk.....	2 oz. (62.2 gm.)
Water	8 oz. (248.8 gm.)
Sugar	300 grains (19.5 gm.)
Casein hydrolysate.....	120 grains (7.8 gm.)
Protein	3.8 per cent.
Carbohydrate	9.0 per cent.
Fat	2.0 per cent.
20 calories per oz.	

The high carbohydrate content operates favourably in "sparing" the protein in metabolism.

Dried milk (especially by the spray process) has yielded a good product, the protein and fat losing none of their values. Casein, owing to its amino-acid content, including methionine and tryptophane, is perhaps the most important food material at the present time. In some countries casein deprivation has led to pancreatic and hepatic degeneration in infants. As a basis for recuperation in childhood malnutrition it has no equal. Milk protein is a great protector of the liver cells against toxic and lipolytic influences. Protein starvation leads to secondary anorexia; tryptophane (in milk) is accredited with special power of restoring appetite.

RHESUS DISEASE

The literature is vast: the therapeutic bearings are relatively simple. Icterus gravis from this cause implies hepatic, and probably cerebral, damage (kernicterus), and often a minimal degree of anæmia. Heroic measures, e.g. exsanguination-transfusion methods, may be resorted to and a few more infant lives saved, but in these cases the cerebral and/or hepatic damage may reveal unfortunate sequelæ. Undoubtedly favourable immediate and remote results can be expected from transfusion therapy in the hæmolytic anæmia or simple erythroblastæmia arising from rhesus or other iso-immunization group factors. Unfortunately no reliable anticipation of the *type* of foetal response can yet be judged by the maternal serum tests which are, or should be, applied in the later months of pregnancy.

NEONATAL INFECTION

This is profoundly important and still contributes considerably to neonatal mortality. Experienced judgment in diagnosis and skilful treatment may be

dramatically successful. Delay in either will probably lead to disaster. Fever, cough, loose stools, vomiting, diminished sucking, apparent anorexia, a rising pulse, may give rise to suspicion. Isolation in an amply ventilated room and skilled nursing with minimal handling are imperative. Breast milk feeding may be life-saving in the particular circumstances, and weaning must be avoided at all costs. Fluid requirements must be adequate and in special cases supplemented by parenteral methods. Renal flow should not unduly decline or secondary metabolic failure will occur. Dehydration and starvation is a serious combination in a baby; therefore water, sugar and protein supplies must not fail. Supplementary hydrolysate of casein may be of special use in such cases. Chemotherapy, e.g. sulphadiazine alone or in synergic effect with penicillin, is often highly effective and especially in the more common acute respiratory infections in the small baby. Penicillin, 10,000 units six-hourly, is adequate and allows a minimal disturbance of the baby; or four to six times the dose may be given by mouth. Rapid anæmia may occur, and a series of small fresh blood transfusions may decide a favourable course.

HÆMORRHAGIC DISEASE OF THE NEWBORN

The relationship of this disease to a special tendency to hypoprothrombinæmia during the first six days of life is now well known. It was hoped that injections of vitamin K at or soon after birth would entirely prevent the disease or rapidly cure it if established. This, however, is not universally effective (although it must be given), and recently it has been shown that hæmorrhage may also occur from a deficiency in other factors closely allied to prothrombin, at present known as factors 5 and 6 (Quick, 1947). It is in such cases that transfusion of fresh blood to the infant may also be called for in order to adjust all the offending deficiencies. Probably this therapy is preferable in all but the mildest cases. Therefore in a case of some severity intravenous blood transfusion should be given, bearing in mind that should the baby be a female it will be necessary to determine her Rh type, since transfusion of Rh-positive blood even to an Rh-negative baby may result in permanent sensitization to the Rh-antigen. In the past it has been customary to give subcutaneous or intramuscular injections of blood, but it is doubtful if the infant's deficient prothrombin, and possibly other defects, can be corrected by this route; and even *via* this route the possibility of sensitization of the Rh-negative female baby by the intramuscular injection of Rh-positive blood must be borne in mind.

GASTRO-ENTERITIS

The exact etiology is still obscure. Virus disease has been considered a possibility; others relate the alimentary disorder to upper respiratory infection, including otitis media, by way of cause or effect. Whichever it is, a careful examination of the upper respiratory tract and ears is necessary, followed by

local treatment when required. In such cases systemic penicillin is desirable, and when renal function is safely assured sulphonamides may be given. The rapid disturbances in water and electrolyte balance call for careful and skilled management of fluid and salt supplies, bearing in mind especially the ease and speed of the development of fatty liver and renal changes, and toxic visceral effects generally. It is wise to anticipate such disastrous possibilities as acute liver swelling, icterus, abdominal distension, and purpura, by maintaining an early and adequate supply of proteins, such as a casein preparation in company with ample carbohydrates (e.g. casein soluble or hydrolysate). In severe cases the daily basal protein requirement may be administered intravenously by using a $2\frac{1}{2}$ per cent. solution of "casydrol", of which 50 c.cm./lb. would provide 1 gm./lb. amino-acids. If plasma is used it is wise to choose this from a single donor in order to minimize the possibility of homologous serum hepatitis. Gastro-enteritis certainly calls for frequent and careful scrutiny of the clinical progress and a knowledge of the probable biochemical requirements, e.g., if gastric vomiting predominates, possible alkalosis is a menace; severe diarrhoea may lead up to acidosis and potassium loss. Dextrose-saline-hydrolysate may remedy the former, but special solutions, e.g. Hartman's, may be required in the latter. Every case must be handled on its merits, bearing in mind that it is always a potentially serious disease, and recognition of probable special requirements should be assessed early and arrangements made accordingly. In severe intractable cases which fail to maintain improvement, and especially when vomiting continues, aural and possibly mastoid disease should be borne in mind.

STEATORRHOEA

(a) *Cystic fibrosis of the pancreas* is by no means rare: bulky, fatty, sometimes vaseline-like, stools in a baby with a good appetite should arouse suspicion. Lesser degrees may occur and at a later age be related to severe or mild infantilism. Pancreatic enzyme deficiency or absence can be determined in order to confirm that diagnosis. Feeds and diet are arranged to provide high protein and carbohydrate and low fat intake. Milk protein is especially valuable as it may delay some of the pancreatic degenerative processes. (It is of interest that in some African races milk protein starvation has been associated with the development of pancreatic and liver fibrosis.) "Pancreatin" granules are of some value in the general treatment. The supervision of lung infection and a productive bronchiectasis is always menacing and special treatment may be necessary to avoid or delay lung abscess formation. High intake of vitamin A may have some special protective value.

(b) *The celiac syndrome* is a different clinical problem. In this there is no known glandular or digestive enzyme defect, but recent observations suggest that some of the effects, e.g. diarrhoea, abdominal distension and even the steatorrhoea, may be secondarily related to starch intolerance (Andersen,

1947). In fact, treatment with starch-free diet may be so satisfactory as to lead to rapid improvement in most of the clinical features, and may at the same time allow a child to ingest some butter daily and to have normal stools. This is certainly an interesting and probably important advance in handling the ever tricky problem of coeliac disease. Since vitamins A and D are absorbed more optimally when dispersed in an "oil in water" system, oil preparations of these vitamins should be made up in a fine dispersion (Sobel *et al.*, 1948). Folic acid may benefit a macrocytic anæmia (which is uncommon) but has no other definite favourable effects. Injection of concentrated "vitamin B complex" has not maintained its alleged miraculous effects (Paterson *et al.*, 1944; Allibone, 1945-6). When vitamin B is given, unilateral overdosage should be avoided; otherwise the members of this group may fail to act as a physiological team. If the basal supply of the B group vitamins is deficient, the excessive addition of one factor of the B complex without the others may accentuate a deficiency of nicotinic acid and riboflavine.

CONGENITAL ABNORMALITY IN THE ALIMENTARY TRACT

(a) *Oesophageal atresia* or stenosis is recognized by either vomiting and/or coughing during or immediately after the first or subsequent feed in *the first twenty-four hours of life*. Accurate and urgent diagnosis is imperative in order that successful surgical treatment can be carried out. A small amount of lipiodol introduced into the œsophagus will define the abnormality. Brilliant results are now obtainable by local reconstructive surgery.

(b) *Congenital duodenal stenosis* may clinically simulate pyloric stenosis but bilious vomit indicates the duodenal abnormality. Projectile bilious vomiting with epigastric peristalsis and no pyloric tumour should lead to a quick diagnosis and an urgent appeal for surgical approach (always aided by the physician's active cooperation regarding fluids, feeding, and the like). Laparotomy may show either a simple atresia or a stenosis due to periduodenal peritoneal adhesions over the third part of the duodenum. In the latter case there is usually also an associated malrotation of the mid-gut (Ladd and Gross, 1941). Excellent clinical cure is now obtainable.

(c) *Pyloric stenosis*.—Two factors dominating safe prognosis are breast feeding and early diagnosis. Too many babies are still given "medicines" for vomiting, or worse still, taken off the breast "because it doesn't suit"! Ward sisters spend days and days trying to restore the breast secretion in some of these unwarranted weanings. If a baby has gastric vomiting and visible epigastric peristalsis he probably has pyloric stenosis. The pyloric tumour is sometimes quite difficult to detect even by an expert. Late diagnosis with accompanied severe dehydration, alkalosis, and possibly tetany, may be dangerous. Quick adjustment of these disturbances with saline-dextrose fluids is essential. Rammstedt's pylorotomy is the desirable aim, especially when short-stay hospital treatment is indicated. Medical measures are usually limited to specially selected cases in which, although

a tumour is palpable, vomiting is not leading to loss in weight or other undesirable effects. Eumydrine (methyl-atropine-nitrate) should not be used indiscriminately as it may have disturbing secondary influences elsewhere. A new preparation, "skopyl" (methyl-scopolamine-nitrate), has been used in Scandinavia and favourable results are reported (Elgenmark, 1945).

SOME OTHER CONGENITAL ABNORMALITIES

Choanal stenosis.—Babies normally nose-breathe. They must do so in order to survive the mechanical intricacies of liquid feeding and the "infant swallow". Choanal atresia or stenosis may be suspected when a baby chokes, gulps, and suddenly stops feeding to take a breath. There is also a characteristic respiratory form with marked inspiratory indrawing of the lower chest. Feeding the baby face forwards may assist in the delicate manoeuvre of feeding and breathing through the same orifice. Localization and treatment of the choanal stenosis is proceeded with at a suitable time and usually with excellent eventual results (Evans, 1948).

Subdural hæmatoma.—In so far as it may occur at or from birth, this may be regarded as congenital in the young baby. An enlarging head with some appearance suggesting hydrocephalic change, bulging fontanelle, vomiting and possibly convulsions, suggest the possibility. Exploration of the subdural space with a needle introduced at the lateral angles of the anterior fontanelle may easily confirm the diagnosis when yellowish blood-stained fluid is aspirated; expert neurosurgical treatment may be called for if simple aspiration is not fully effective.

BRONCHIECTASIS

An attitude of *laissez faire* should be abandoned and every case should be subject to an elaborate and meticulous diagnostic schedule regarding position, extent and type of the disease and all associated facts, e.g. nasal sinus sepsis, other lung disease, respiratory exchange and the presence or absence of emphysema. The aim in the established case is to proceed to removal of all the affected tissue after a suitable and accurately supervised period of preparation. Surgery offers excellent results provided the preoperative phase includes clearance of lung and nasal sepsis. The surgeon removes only that lung tissue which is affected, thus sparing all the normal lung possible in order to avoid undesirable compensatory emphysema thereafter. Follow-up respiratory exercises establish normal thoracic form and movement. Sequence of action is therefore clear, and when surgical treatment is impossible simple postural drainage must be a regular daily routine. Penicillin aerosols are of some value but sterilization of the infected cavities can rarely be achieved.

ASTHMA

It must be borne in mind that "asthma" is a symptom related, in children,

to several factors, e.g. constitution, respiratory infections, nervousness, fatiguability, anxieties and a host of other possibilities. Complete survey of the child's physique and temperament and the social environment is necessary in assessment; elimination of the several contributory causes is essential in the treatment. A study of the family is often necessary. Whilst asthma may start with a simple cause it is often continued by psychogenic additions, especially in the sensitive, emotionally labile, intelligent child. Attendance to the child's way of life, exercise and rest, body weight and general nutrition, respiratory hygiene and method, confident endeavour and an inculcation of an understanding approach to health and elimination of fear, and a raised resistance to respiratory infection will operate additively. The cycle—fatigue→irritability→anorexia→increased fatigue→nervousness, a "cold"→descending tracheobronchitis→bronchiolitis→"asthma"—is only too evident in the child round about five to seven years of age who is negotiating his early school life under stresses of an emotional, physical and possibly intellectual order. A kindly searching clinical approach is therefore of fundamental importance and a fatalistic attitude or an overdominance of symptomatic and drug treatment should be avoided. Personal disaffinities can wreck this type of child. Recent research in drug therapy suggests that isopropyl-adrenaline, which can be given perlingually, may be useful, thus avoiding injection therapy (Herxheimer, 1948). Current opinion is divided on the value of antihistamines, e.g. "anthisan" or "neoantergan", but oral use may be tried. In "acute asthma" due to acute bronchiolitis the infection should be attacked by sulphonamides or penicillin: dramatic relief may occur as the infection is so inhibited. As a preventive or curative measure in asthmatic children respiratory exercises, with special reference to full diaphragmatic excursion, are of great value. The *general health* must be kept at as high a level as is possible, and alleged "allergens" and "desensitizing techniques" not allowed to smother the child with therapeutic enthusiasms.

SUBNORMAL HEALTH

This is an important diagnosis. Subnutrition, especially protein insufficiency, hypochromic anæmia, chronic upper respiratory sepsis, anorexia, insomnia, chronic fatigue arising out of late hours and incessant daily activity, all call for a rational approach in treatment, which may, in a preventive sense, anticipate and avoid a catastrophic breakdown, e.g., acute rheumatism, chorea. In chronic infections it is essential to supply a liberal protein intake in order to counter the tendency to negative nitrogen balance. This also applies to rehabilitation after acute infections or injuries.

ACUTE OSTEOMYELITIS

Advances in treatment have greatly altered the course of this disease. Early diagnosis is, however, the key-note. Penicillin administered within

twenty-four hours is likely to abort the disease entirely. Delay, even for a further day, may considerably magnify the local bone disease, but fortunately, even so, nothing more than aspiration of abscess material may be required. In babies, acute osteomyelitis may spread seriously and almost silently so that the bone is quickly bathed in pus. Surgical cooperation will be necessary in so far as bone drilling or treatment of an abscess is necessary. Penicillin must be continued until all evidence of blood-stream and local infection has disappeared, and any dangers of pyæmic dissemination and especially of pericarditis are passed. Sulphathiazole should be given as an extra weapon of attack against the *Staph. aureus*, and when toxic anæmia occurs fresh blood transfusions may be of great value. In a recent series the most satisfactory results were obtained by 500,000 units of penicillin daily over a period of twenty-eight days, together with early simple metaphysial decompression (Tucker and Hallenberg, 1948).

ACUTE POLIOMYELITIS

In many cases an "initial" illness, with an upper respiratory infection, coryza or irritable tonsillitis and pharyngitis, occurs and precedes the onset of meningo-neural signs by a few days or a week or so. In seasonal epidemics of poliomyelitis it is desirable therefore to keep the child with this suspected "initial" disorder in bed, in order to minimize muscular activity. Recent observation suggests that the damaging effects of the virus on the nervous system are thus rendered less potent. In any event, when suspicious early "pre-paralytic" symptoms, e.g. pains in the limbs, backache, are evident, it is an urgent necessity to place the child at absolute rest. Exercise at this stage may encourage widespread virus invasion of the motor nervous system with consequent paralysis. Therefore whilst at present there is no specific remedy against this virus, every clinical attention must be paid to the suspicious "initial" or to the prodromal symptoms and complete rest for seven to ten days enforced. Muscular action in some way increases susceptibility and localization of the virus in the corresponding neural spinal centres (Russell, 1947).

MENINGITIS

It is in this group of diseases that spectacular advances in treatment have been made. In a child with meningeal signs the causative factor must be determined as soon as possible. The clinical history may be a useful guide, but accurate assessment must depend upon examination of the cerebro-spinal fluid—biochemistry, cells and bacterial content.

Acute meningococcal meningitis of average degree will respond favourably to sulphonamide therapy. Special cases require more elaborate management. Young children may be particularly susceptible to meningococcal disease, toxic action causing vomiting and diarrhœa; intravenous drip treatment including soluble sulphonamide may be necessary in the first forty-eight

hours. A careful watch must be kept for collapse and other evidence of acute adrenal failure; serious cases may be given an injection of adrenocortical hormone, e.g. 2-5 mgm. of DOCA, as a precautionary measure. Penicillin treatment may also be used, especially when blood-stream infection is suggested by considerable purpuric eruption.

Acute pneumococcal meningitis.—Special suspicion will arise when otitis, or sinusitis precedes acute meningitis, but a glance at the cerebrospinal fluid under a microscope will usually reveal numerous pneumococci. A delay in diagnosis by one day may be disastrous. Thick meningeal pus quickly forms and renders approach by antibiotics difficult. Heroic therapy is required in this form of meningitis. Pure penicillin, up to 10,000 units, should be given intrathecally each day and supported by systemic penicillin in large doses. Synergic actions with oral sulphonamide should also be implemented. A heavy attack is necessary over the first four days at least, in order to assure effective destruction of the pneumococci. Quick, favourable response and complete cure may be seen in the early case. However, pneumococcal meningitis is often a fulminating and very dangerous disease, the toxins being especially active in the nervous system.

Influenzal meningitis.—Apart from epidemics, this is almost as common as the meningococcal disease. There are several types of *H. influenzae* responsible. Type B is the most common and fortunately the most susceptible to modern therapy. It is important to obtain urgent bacteriological diagnosis and a typing of the *H. influenzae* in regard to its particular susceptibility to sulphonamide, penicillin or streptomycin. Most are streptomycin sensitive, many are sensitive to penicillin and some are sensitive to sulphonamide alone. Particular means of treatment will depend upon these facts, but when the answers are not quickly obtainable it is desirable to proceed to intrathecal streptomycin injections in combination with systemic treatment and sulphonamide by mouth. When streptomycin is not available, pure penicillin should be given by the lumbar route. The treatment must be continued until the general signs have disappeared and the cerebrospinal fluid is quite sterile. There is some danger of relapse if treatment is prematurely discontinued. Prognosis, like that of the meningococcal or pneumococcal disease, may be favourable, but, again, delay in diagnosis may quickly lead to a refractory state through an impassable gelatinous exudate in the basal subarachnoid cisternæ.

Bacillus coli meningitis is usually seen in babies under the age of three months, and probably arises from neonatal bacteraemia or inhalation of infected amniotic fluid. Fits, a bulging fontanelle, and a purulent cerebrospinal fluid containing the organism, confirm the diagnosis. Some strains of *B. coli* are destroyed by sulphonamide, but streptomycin therapy is usually necessary to obtain effective improvement.

Tuberculous meningitis.—A new and urgent responsibility has been thrown upon the practitioner. This disease must now be diagnosed probably within

the first week in order to render effective the new and powerful remedy, streptomycin. There is no doubt that the tubercle bacilli can be inactivated and probably destroyed by this substance, provided (a) that the subarachnoid system is in free communication and loculi are absent, and sequestration of bacilli has not occurred as a result of leptomeningeal thickening and occlusions; (b) that a tuberculoma of the brain is not discharging bacilli repeatedly into the meninges; (c) that the bacilli are not present in overwhelming numbers. From the earliest days of the disease inflammatory occlusive changes may occur in the cerebral and meningeal arterioles, and this may most seriously affect the prognosis if treatment is delayed. Every practitioner should therefore be fully aware of the earliest clinical evidence of tuberculous meningitis if a possible curative result is to become available to the patient. The technique of treatment is elaborate and prolonged and necessitates hospital accommodation, especially as streptomycin is given intrathecally at daily intervals in the first instance. Individually the clinical results leave no doubt that recovery can occur, but it would be unwise to speak dogmatically at this stage. A prolonged follow-up period of observation is required to assess possible remote sequelæ and any relapse incidence. It is of interest to know that miliary tuberculosis may respond favourably, if slowly (as revealed by radiology of the lungs), and that choroidal tubercles may pass on to a stage of resolution under the influence of streptomycin. The use of this substance in other forms of childhood tuberculosis has not yet been assessed. It is most necessary to hold streptomycin in central control for the present because its indiscriminate use may engender the development of insensitive strains.

PROPHYLACTIC THERAPY

No authoritative report from this country is yet available on the use of B.C.G. vaccine in protection against *primary tuberculosis* in childhood. Scandinavian reports continue to be optimistic in their evaluation of the protective treatment (Wallgren, 1947). For the time being vigilance in protecting children in contact with open tuberculous disease in adults must remain the main defensive operation. In *pertussis*, prophylactic vaccine therapy has not proved significantly valuable, but continued trial should be made with potently antigenic vaccines at 100,000 million organisms as the average dose. Protective treatment against *measles* with concentrated placental globulins or gamma globulins may be regarded as the safest method of conveying passive immunity; unfortunately there is no known curative remedy in measles, which awaits with most of the other virus diseases the discovery of a viricidal antibiotic.

EPILEPSY

Electroencephalography has yielded helpful evidence on the diagnostic pattern and incidence of latent or manifest cerebral dysrhythmia, and thus

may give a guide on the effects of certain general forms of treatment and the actions of special drugs. Low fluid and low salt intake may lessen the incidence of attacks and at the same time potentiate the therapeutic effect of small doses of bromide or barbiturate. The ketogenic diet treatment also operates through the combined effects of slight tissue dehydration and the cerebral sedative effects of the ketones. It is of importance to realize that behaviour disorders in children may manifestly be the personal expression of an encephalographic abnormality and may similarly respond favourably to treatment. An unexpected observation is the beneficial effect of benzedrine, alone or in combination with a barbiturate, in some of the juvenile cases. An important aspect of epilepsy in childhood is the avoidance of fear and anxiety which may gradually lead to despair and social isolation, especially when unwise parents indulge in persistent apprehension instead of accepting the situation logically and helping to develop their child along normal healthy lines of character, confidence and ability. The sense of invalidism and inferiority sometimes engendered by mismanagement of the child's whole problem is deplorable.

PSYCHOLOGICAL TREATMENT

Improved working arrangements between pædiatricians and psychotherapy departments has brought about an advance in the necessary team work for treatment of the common functional disorders in children. Enuresis, encopresis, nervous aggravation of some allergic disorders, behaviour problems, all form an important field for most helpful cooperative effort and one which may produce abundant satisfaction to the parents, and thereby an improved mental approach to these harassed and harassing juveniles. Social pædiatrics has some of its most fruitful results in these circumstances. A study of the juvenile mind and its amazing labilities is a matter requiring the most careful adjudication by the supervising practitioner when called upon to treat psychosomatic problems in childhood. As a bearing on the "psychologically abnormal child" or upon "speech difficulties" careful assessment of any aural and visual disorder is essential. Alarming diversions of character and apparent incompetency may arise out of unsuspected zonal deafness (as detected by audiometry), from ocular strain, sense of inferiority or insecurity, chronic fatigue, or minor grades of "spastic" muscular executive disorder.

DRUGS

Penicillin.—Oral penicillin has received careful trial (Coblan *et al.*, 1948), and is a useful method in babies and young children. Adequate blood levels can be achieved provided about four times the usual injection dose is prescribed, preferably given 20 minutes before a feed or $2\frac{1}{2}$ hours after the previous feed. Penicillin in children may for special reasons demand less

frequent injections and it is clinically true that larger doses at six- or eight-hourly intervals provide quite a suitable routine. Crystalline penicillin is used in concentrated solution suitable for intrathecal purposes and is a valuable remedy in pneumococcal and in some cases of influenzal meningitis.

Calciferol.—Vitamin D₂ is a potent anti-rachitic vitamin which can be prescribed in a single large dose, e.g. 50,000 units, as an initial step in treatment of rickets. In the uncommon cases of "refractory rickets" similar large doses may need to be continued daily over several weeks before any evidence of healing is seen. It has been suggested that high dosage with calciferol might aid healing of tuberculous glands: this remains undecided, but is worth a trial. Nausea, anorexia, vomiting and other symptoms may indicate that toxic levels have been reached and the dosage must be reduced. Calciferol is especially useful in maintaining adequate vitamin D function in the necessarily restricted fat diet in steatorrhœa. In premature babies 1000 units daily will ensure adequate calcium and phosphorus absorption from the bowel and so facilitate satisfactory bone development.

Sulphonamides.—Under conditions in which oral or intravenous administration is not possible the desire for a neutral soluble sulphonamide which could be injected intramuscularly has now been satisfied by the introduction of "soluthiazole". Experimental and clinical trials have given satisfactory results. The solution is hypertonic and therefore should not be given subcutaneously or in relation to serous or mucous membranes (Banks, 1947). It is of some importance to know that sulphathiazole may precipitate an attack of erythema nodosum in a child who is suffering from a primary tuberculous infection.

Antispasmodics.—Methyl-atropine-nitrate (eumydrine) has its uses in pyloric narrowing or spasm and has given some satisfaction in asthma in infancy. An 0.6 per cent. alcoholic solution contains 0.1 mgm. per minim; 2 to 3 minims (0.12 to 0.18 c.cm.) sublingually, 15 minutes before food, may be effective. Methyl-scopolamine-nitrate is alleged to have eight times the potency of eumydrine and to have no side-effects (Elgenmark, 1945). Octyl-nitrite as an inhalant has given distinct success in certain spasmodic disorders of the œsophagus. Occasionally glyceryl trinitrate, grain 1/400 (0.16 mgm.), is highly effective in overcoming sphincteric spasm (Falle, 1948) or peripheral arterial difficulties in some forms of polyarteritis. Methyl-ephedrine is considered to have less vasopressive effects than ephedrine and may be of particular value in enuresis or asthma, owing to its more prolonged relaxant effect on certain smooth musculature. Isopropyl-adrenaline (aleudrine or neo-epnine) has special clinical value in the treatment of bronchiolar spasm and is effective as a tablet, 0.02 gm., sublingually, or as a 1 per cent. atomizer spray (Herxheimer, 1948; Dunlop and Hunter, 1948). It is alleged to have a greatly increased relaxing effect on bronchial muscle in five minutes while causing minimal effect on the circulation and no rise in blood pressure; overdosage, however, may produce adrenaline-like effects.

ADVANCES IN PÆDIATRICS

Antihistamine preparations.—In certain urticarias, angioneurotic edema, and possibly in juvenile asthma, this group of drugs may produce marked clinical results are somewhat equivocal. Benadryl has disadvantages. This is much less so with "anthisan" (pyranisamine), but its use must be correlated with the age and responses of the child (Hershey, 1948). Considerable success has been achieved in allergic rhinitis in children using 0.1 gm. t.d.s.

Sedatives.—Phenobarbitone is well tolerated by babies and is given in $\frac{1}{8}$ – $\frac{1}{4}$ grain (8–16 mgm.) doses, e.g., shortly before the bedtime dose. Sodium phenytoin occupies a stable place in the anti-epileptic group. It is now in the official list. Tridione, of special use in *petit mal* (Lennox, 1946), remains under clinical trial, and should be abandoned if excessive sedation, visual halos, toxic rashes or agranulocytic tendencies appear. Chloral hydrate (muscular paraldehyde (1–4 c.cm. according to age) is a valuable sedative in children.

References

- Allibone, E. C. (1945–6): *Proc. Roy. Soc. Med.*, 39, 700.
 Andersen, D. (1947): *J. Pediat.*, 30, 564.
 Banks, H. S. (1947): *Lancet*, i, 45.
Brit. Med. Bull. (1947): 5, 1099.
 Calder, A. G. S. (1948): *Lancet*, i, 863.
 Coblan, et al. (1948): *Amer. J. Dis. Child.*, 75, 15.
 Crosse, V. M. (1945): "The Premature Baby", London, p. 14.
 Dunlop, D. M., and Hunter, R. B. (1948): *Lancet*, i, 849.
 Elgenmark, O. (1945): *Acta. Pædiat.*, 32, 371.
 Evans, P. R. (1948): *Proc. Roy. Soc. Med.*, 41, 454.
 Falle, E. C. (1948): *Lancet*, i, 794.
 Gordon, H. H., and Levine, S. Z. (1947): *Amer. J. Dis. Child.*, 73, 442.
 Herxheimer, H. (1948): *Lancet*, i, 667.
 Ladd, W. L., and Gross, R. E. (1941): "The Abdominal Surgery of Infants and Children," London.
 Lennox, W. G. (1946): *J. Pediat.*, 29, 356.
 Miller, F. J. W. (1947): *Arch. Dis. Child.*, 22, 54.
 Paterson, D., et al. (1944): *Ibid.*, 19, 99.
 Quick, A. J. (1947): *Lancet*, ii, 379.
 Russell, W. R. (1947): *Brit. med. J.*, 2, 1023.
 Sobel, A., et al. (1948): *J. Nutrit.*, 35, 225.
 Tucker, A. R., and Hallenberg, C. (1948): *Lancet*, i, 701.
 Waller, H. F. (1946): *Arch. Dis. Child.*, 21, 1.
 Wallgren, A. (1947): *Sven. Nat. Foren. Tuberkulose Kvartals.*, 42, 17.

ADVANCES IN CARDIOLOGY

By CRIGHTON BRAMWELL, M.D., F.R.C.P.

Professor of Cardiology, Manchester University.

The most outstanding recent advances in the treatment of heart disease are the control of infection in subacute bacterial endocarditis by penicillin, the elimination of certain congenital lesions by operation, and the prevention of thrombo-embolic complications of cardiac infarction by anticoagulants.

SUBACUTE BACTERIAL ENDOCARDITIS

When penicillin first became available in Britain it was in short supply, and consequently its use was restricted to those conditions in which its beneficial therapeutic effect was already established. The earlier reports of its value in bacterial endocarditis were extremely disappointing and, in 1944, Keefer stated that of 55 cases treated in the United States three only were alive a year later. Early in 1945, the Medical Research Council initiated a co-ordinated investigation on the subject and a summary of the results obtained was published by Christie in January 1948. Early in this investigation it became evident that the duration of treatment was of great importance.

In a group of 52 patients, all given 5 mega-units, 83 per cent. relapsed or died infected when the period of treatment extended over only five days, as compared with 50 per cent. who were given the same total quantity of penicillin over a period of ten days, and 22 per cent. when the period was twenty days. Later it was found that a dose of 0.5 mega-unit daily for twenty-eight days was sufficient to control the infection in 90 per cent. of patients, although about 35 per cent. of these subsequently died of heart failure or other complications. In cases in which the infecting organism is highly resistant to penicillin, we now give 2 mega-units daily over a period of six to eight instead of only four weeks, but we have not yet made sufficient observations to assess the efficacy of this dosage.

In my own clinic, it has been our experience that the drug is better tolerated when given by three-hourly intramuscular injection rather than by continuous intramuscular drip. In successful cases the temperature falls to normal within two or three days of starting treatment, but often rises again at the beginning of the second week, an intermittent pyrexia persisting until the end of the course of penicillin therapy, when the temperature falls to normal. This is not due to failure to control the infection, but is merely a drug fever. The patient should always be confined to bed for three weeks after the end of treatment. Carefully graduated bed exercises are then started, and about ten days later he is allowed up for a short time. To prevent heart failure great care is necessary during the early period of rehabilitation, however well the patient may appear to be.

Although infection can usually be controlled by a single course of treatment with penicillin lasting for only twenty-eight days, it takes much longer for the sedimentation rate, the anæmia and the weight to return to normal. In our successful cases the sedimentation rate did not reach normal until

about five weeks after the completion of treatment. Often there was little rise in hæmoglobin during treatment and a normal level was not attained until about three months later, whilst a gain in weight continued up to nine months after treatment. The convalescence of these patients is slow and requires careful management. The average period in hospital was fourteen weeks, and full activity was not resumed until six months later.

Of the first 33 patients treated at the Manchester Royal Infirmary, 15 died and 18 are alive two years or more after completion of treatment. There were no relapses in this series, but two patients were later reinfected with a different organism. Both responded satisfactorily to treatment. Christie's analysis showed that 90 per cent. of relapses occur within one month of completion of treatment. Of our 15 deaths, 8 occurred during or within a few days of the completion of treatment, and the other 7 within the next four months. Heart failure developed in nearly half of our patients and was the principal cause of death in two-thirds of the fatal cases. In fact, recovery was the exception in patients who developed heart failure and the rule in those who did not. Major embolic phenomena—cerebral and pulmonary embolism—were responsible for 3 of our 15 deaths. Of the 18 patients who recovered, 15 were able to resume their former occupations. In the other three cases deterioration appears to have been due to the additional burden thrown upon the heart by a stenotic valvular lesion which increased in severity after the infection had been controlled, in fact, in the process of healing.

In our experience, the most important factor in prognosis is the duration of symptoms of infection before the institution of treatment. When symptoms have been present for less than ten weeks the prognosis is much more favourable than when it has been present for twenty weeks or more, and there is good reason to believe that the present mortality can be reduced by earlier diagnosis. This is not easy, for the initial symptoms of the disease rarely give any indication of the nature of the infection, and it is therefore important that in every case of unexplained pyrexia, especially if there be an associated heart lesion, a blood culture be taken without delay. Also, since the pre-existing heart lesion is generally of a trivial nature, if treatment be instituted before the infection has had time to produce further damage, we may hope to render the patient fit to resume his former occupation. Apart from the duration of infection, prognosis is influenced by the age of the patient, the mortality being higher in those over fifty and, as Christie (1948) has pointed out, by the state of nutrition.

CONGENITAL HEART DISEASE

It is less than ten years ago that Gross and Hubbard (1939) reported the first successful operation for closure of the *patent ductus arteriosus*. This has now become a well-established surgical procedure which merits favourable consideration in all cases, since it eliminates the danger of infective pulmonary arteritis, relieves the strain thrown on the heart by the arterio-venous fistula and, even in children who show little evidence of cardiac embarrassment, leads to a gratifying gain in weight and general well-being.

In 1947 Shapiro collected information regarding 626 patients treated surgically. In 195 of these the ductus had been divided: in the other 431 it was ligated. The

former is a more difficult operation, but it eliminates the possibility of recanalization, and in skilful hands does not appear to carry a higher mortality than ligation. Of 431 patients treated by ligation the mortality in 343 uninfected cases was 4.9 per cent., and in 88 infected cases 28.4 per cent., a low figure considering that many of the infected cases were operated on before the introduction of penicillin treatment. In 195 cases in which the ductus was divided there were only 3 deaths. Thirteen of these cases were infected.

Provided infection has not become generalized, it can be controlled by closure of the ductus; but in seriously ill patients a preliminary course of penicillin lessens the operative risk.

When the typical machinery murmur is present, the diagnosis of patent ductus presents little difficulty, other conditions, such as cardio-aortic fistula, which give rise to a similar murmur being extremely rare; but when only a systolic murmur is present, diagnosis is less certain, and in these circumstances opinion is divided regarding the justifiability of operation. Other physical signs supporting the diagnosis of patent ductus are enlargement of the pulmonary artery, a water-hammer pulse, and a fall in diastolic pressure following exercise.

In the course of some experimental observations on closure of the patent ductus in dogs, Crafoord (1945) had occasion to clamp the aorta. This procedure was so surprisingly well tolerated that it led him to consider the possibility of resecting the stenosed segment in *coarctation of the aorta*, an astonishing surgical feat which he first accomplished in 1944, since when several successful cases have been reported from other clinics.

Many patients with coarctation of the aorta die of congestive heart failure or of bacterial endocarditis: some, however, are symptom-free, but even in their case operation is worth considering, for they are exposed to the risk of sudden death from rupture of the aorta. Patients under thirty years of age are most suitable for this operation, since in older subjects the aortic wall is apt to be the seat of degenerative changes which render apposition of the cut ends of the aorta more difficult.

The diagnosis of coarctation of the aorta is easy, provided the possibility of its occurrence be kept in mind in all cases of unexplained hypertension. Feeble or absent pulsation in the femoral arteries, pulsating arteries on the front or back of the chest, a systolic murmur of unusual distribution and notching of the ribs, as shown by radiography, are the most obvious features. The stenosis can be clearly demonstrated by angiocardiography.

The brilliant work of Blalock and Taussig has naturally attracted much attention, not only in the medical but also in the lay press, and this has led many parents to hope that their children may be cured. Unfortunately not all "blue babies" are suitable for the Blalock operation.

Cyanosis, in congenital heart disease, is due to mixture of the venous blood in the right heart with arterial blood in the left, a right to left shunt being established through an aperture either in the ventricular or in the atrial septum. Defective blood supply to the lungs is an important contri-

butory factor in some cases. Children born with a gross cardiac abnormality such as bilocular or trilocular heart rarely survive infancy: the majority of "blue babies" who do survive exhibit *Fallot's tetralogy*. This is a combination of congenital defects, including pulmonary stenosis and an aorta which overrides the ventricular septum and so communicates with both ventricles. Clinically, a defect in the ventricular septum with dilatation, instead of stenosis, of the pulmonary artery (the Eisenmenger complex) may resemble Fallot's tetralogy, although cyanosis and finger clubbing are less pronounced. It is important to distinguish between the different congenital defects which may be associated with cyanosis, for the object of Blalock's operation, which consists in establishing an artificial ductus, is to increase the blood supply to the lungs, and unless this be deficient the operation serves no useful purpose. In Fallot's tetralogy, owing to the pulmonary stenosis, very little blood reaches the lungs, and by improving the pulmonary circulation the oxygen content of the arterial blood can be greatly increased and the cyanosis relieved.

Radiology plays an important part in the diagnosis of Fallot's tetralogy. The left heart border is concave in its upper part and the heart is boot-shaped, the usual prominence due to the pulmonary conus being absent: the lung fields are clear and the root shadows inconspicuous. Prominence of the pulmonary arc, congestion of the lung fields or pulsation of the hilar shadows negative this diagnosis. The most suitable subjects for operation are children between two and fifteen years of age in whom there is little, if any, cardiac enlargement. In Fallot's tetralogy the electrocardiogram always exhibits right axis deviation, and in this respect differs from congenital atresia of the tricuspid orifice.

Two laboratory procedures—catheterization of the heart, and angiocardiology—have proved helpful in establishing the diagnosis of various congenital heart lesions. *Catheterization* enables us to compare not only the oxygen saturation of the blood in the right auricle, right ventricle and pulmonary artery, but also to measure the pressure in these situations. If the oxygen saturation in the right auricle is considerably higher than in the superior vena cava, the presumption is that oxygenated blood from the left auricle has been added to the venous blood in the right auricle through a defect in the atrial septum. A similar difference between the blood in the right auricle and right ventricle suggests a ventricular septal defect, whilst a higher saturation in the pulmonary artery than in the right ventricle indicates a patent ductus. The diagnosis of pulmonary stenosis is established by finding on catheterization that the pressure in the right ventricle is higher than that in the pulmonary artery, and finally the passage of the catheter through an abnormal aperture may be recognized by fluoroscopic control.

In *angiocardiology*, the intravenous injection of a radio-opaque substance—diodrast—permits visualization first of the right and then of the

left side of the heart and recognition of abnormal communications between them.

In *Blalock's operation* the pulmonary artery is anastomosed to the innominate or right subclavian artery (or to the left subclavian in cases with a right-sided aorta), whilst in *Pott's operation*, which serves a similar purpose, the anastomosis is between the pulmonary artery and the aorta. In about 70 per cent. of cases the therapeutic result of these operations is truly dramatic; not only is there an almost miraculous improvement in the exercise tolerance, but the rapid bodily and mental development of the child is remarkable. In Taussig's (1947) first 300 cases, the operative mortality was only 18 per cent. Sufficient time has not yet elapsed to allow of an assessment of the ultimate prognosis in these cases, nor to say how well the heart will tolerate the additional strain thrown upon it by the artificial ductus, but the immediate result is astounding.

Still more recently Brock (1948) and Sellors (1948) have reported promising results from an operation designed to enlarge the pulmonary orifice, by section of the valve, in cases in which the stenosis is localized to the valve itself and is due to obstruction of the pulmonary orifice by a septum formed by fusion of the valve cusps.

The great advance in recent years in the technique both of thoracic surgery and of anæsthesia would not have made these surgical procedures possible but for the preoperative and postoperative therapeutic measures now available, of which penicillin and the anticoagulants deserve special mention.

ANTICOAGULANT THERAPY IN CORONARY THROMBOSIS

The use of anticoagulants in acute thrombophlebitis and as a postoperative prophylactic measure to prevent pulmonary embolism is well established. Its application to the treatment of myocardial infarction following coronary thrombosis is a more recent development, but statistics published by Parker and Barker (1947) and other American workers suggest that anticoagulant therapy materially reduces the mortality rate and the incidence of thrombo-embolic complications. The importance of these complications as a cause of death in cardiac infarction does not appear to have received sufficient recognition in Britain.

The drugs used are heparin and dicoumarol. *Heparin* is given intravenously and has the advantage that it acts quickly, but its action is transient, even a large dose being effective for only about six hours. *Dicoumarol*, which is given by mouth, does not develop its full action for about forty-eight hours, but is effective for a much longer time than heparin, and incidentally is much cheaper. Dicoumarol, however, is a dangerous drug. It should never be given to a patient at home, but only in hospital, where facilities are available for controlling treatment by repeated prothrombin estimations; for, if the prothrombin concentration falls below 20 per cent.,

serious hæmorrhage may occur. It is important to distinguish clearly between prothrombin time and prothrombin concentration, since the relation between them is not linear, but varies with the technique employed. When used as a prophylactic measure the aim is to maintain the prothrombin concentration at between 20 and 30 per cent. until the patient has been ambulatory for a few days; but he should not be discharged from hospital until the prothrombin concentration has returned to its normal value of over 70 per cent. In cardiac infarction, anticoagulant therapy should be started at the earliest possible moment and continued for a period of at least four weeks.

The procedure followed in my department, which has been suggested by Dr. R. W. Fairbrother and Dr. H. Lempert, is as follows:—

A specimen of blood for prothrombin estimation is taken at 9 a.m. each day, and if the prothrombin concentration on the first day is below 70 per cent. the case is considered unsuitable for dicoumarol, since this level suggests liver dysfunction. If the concentration is above 70 per cent., an initial dose of 300 mgm. of dicoumarol is given on the first day, and on the following days the dose is adjusted in accordance with the prothrombin concentration. For example, on the second day, if the prothrombin concentration is over 50 per cent., we give 200 mgm., but if it is under 35 per cent. we do not give any. For intermediate concentrations (i.e. 45 to 50 per cent. and 35 to 45 per cent.) a dose of 150 or 100 mgm. is given. On the following days, if the concentration is over 25 per cent., we give 100 mgm.

The anticoagulant action of dicoumarol is augmented by salicylates, and special caution is necessary when patients are taking these drugs.

In the event of serious hæmorrhage from overdosage with dicoumarol, the most effective treatment is transfusion with whole blood. Fresh blood should be used. In addition, nicotinamide, 100 to 200 mgm. daily, combined with ascorbic acid or, alternatively, 60 mgm. of synthetic vitamin K, two-hourly for three doses, may help. Some workers recommend intravenous vitamin K.

To tide over the latent period before dicoumarol is fully effective, 10,000 units of heparin are given on the first two days at 10 a.m. and 2 p.m. and 15,000 units at 6 p.m. and midnight. If the prothrombin concentration on the second day is over 50 per cent., heparin is continued until midnight on the third day. It is important that no heparin be given between midnight and 10 a.m., as it would interfere with the prothrombin estimation the following morning.

References

- Brock, R. C. (1948): *Brit. med. J.* **i**, 1121.
Christie, R. V. (1948): *Ibid.*, **i**, 1.
Crafoord, C., and Nylin, G. (1945): *J. thorac. Surg.*, **14**, 347.
Gross, R. E., and Hubbard, J. P. (1939): *J. Amer. med. Ass.*, **112**, 729.
Keefer, C. S. (1944): *Ibid.*, **124**, 636.
Parker, R. L., and Barker, N. W. (1947): *Proc. Mayo. Clin.*, **22**, 185.
Potts, W. J., and Gibson, S. (1948): *J. Amer. med. Ass.*, **137**, 343.
—, Smith, S., and Gibson, S. (1946): *Ibid.*, **132**, 627.
Sellors, T. H. (1948): *Lancet*, **i**, 988.
Shapiro, M. J. (1947): "Modern Concepts of Cardiovascular Disease." **16**, 1.
Tauszig, H. B. (1947): *Bull. N.Y. Acad. Med.*, **23**, 705.

left side of the heart and recognition of abnormal communications between them.

In *Blalock's operation* the pulmonary artery is anastomosed to the innominate or right subclavian artery (or to the left subclavian in cases with a right-sided aorta), whilst in *Pott's operation*, which serves a similar purpose, the anastomosis is between the pulmonary artery and the aorta. In about 70 per cent. of cases the therapeutic result of these operations is truly dramatic; not only is there an almost miraculous improvement in the exercise tolerance, but the rapid bodily and mental development of the child is remarkable. In Taussig's (1947) first 300 cases, the operative mortality was only 18 per cent. Sufficient time has not yet elapsed to allow of an assessment of the ultimate prognosis in these cases, nor to say how well the heart will tolerate the additional strain thrown upon it by the artificial ductus, but the immediate result is astounding.

Still more recently Brock (1948) and Sellors (1948) have reported promising results from an operation designed to enlarge the pulmonary orifice, by section of the valve, in cases in which the stenosis is localized to the valve itself and is due to obstruction of the pulmonary orifice by a septum formed by fusion of the valve cusps.

The great advance in recent years in the technique both of thoracic surgery and of anæsthesia would not have made these surgical procedures possible but for the preoperative and postoperative therapeutic measures now available, of which penicillin and the anticoagulants deserve special mention.

ANTICOAGULANT THERAPY IN CORONARY THROMBOSIS

The use of anticoagulants in acute thrombophlebitis and as a postoperative prophylactic measure to prevent pulmonary embolism is well established. Its application to the treatment of myocardial infarction following coronary thrombosis is a more recent development, but statistics published by Parker and Barker (1947) and other American workers suggest that anticoagulant therapy materially reduces the mortality rate and the incidence of thrombo-embolic complications. The importance of these complications as a cause of death in cardiac infarction does not appear to have received sufficient recognition in Britain.

The drugs used are heparin and dicoumarol. *Heparin* is given intravenously and has the advantage that it acts quickly, but its action is transient, even a large dose being effective for only about six hours. *Dicoumarol*, which is given by mouth, does not develop its full action for about forty-eight hours, but is effective for a much longer time than heparin, and incidentally is much cheaper. Dicoumarol, however, is a dangerous drug. It should never be given to a patient at home, but only in hospital, where facilities are available for controlling treatment by repeated prothrombin estimations; for, if the prothrombin concentration falls below 20 per cent.,

is also more cumulative. The central and visceral side-effects resemble those of prostigmin, and the latter can be controlled by means of atropine. Prostigmin and T.E.P.P. can be prescribed together.

PENICILLIN IN NEUROSYPHILIS

The value of penicillin therapy in cases of syphilis of the nervous system is ineluctable. But many points of uncertainty and even of dispute in this connexion still exist.

Dosage is not yet firmly established. When penicillin was first employed in neurosyphilis a course of treatment was pegged at about two million units. In subsequent reports the optimum dosage was quoted as higher, the level steadily mounting as one paper after another appeared upon the subject. The total grew from three million to four million; later still to five million and even six million. Hints of second and even third courses appeared. These shifting conceptions of penicillin therapy are somewhat disturbing and recall the initial optimism and subsequent disappointments in the early days of salvarsan. Perhaps the most common total dosage adopted to-day in the treatment of neurosyphilis is a course of five million units.

Method of administration.—The next problem concerns the manner in which this five million total is to be administered. Earlier writers suggested frequently repeated intramuscular doses of moderate size, e.g. 30,000 or 50,000 units every three hours. But later it became more usual to prescribe a single daily dose of 300,000 units for a fortnight. This latter technique obviously possesses many practical advantages if it can be shown to be as good as the older method of frequent small amounts. There is yet another mode of administration, namely to prescribe 600,000 units hourly for five days. In this case the patient needs to be in a clinic or hospital. Attempts have been made to delay the rate of absorption by using penicillin in a beeswax emulsion, but this practice has not yet come into general use. The intramuscular route remains the optimum, and intravenous injections, and continuous drip techniques have no advantages in the treatment of neurosyphilis.

Closely bound up with the details of dosage is the question of untoward *side-effects* of penicillin therapy. These are rare enough to make penicillin the treatment of choice in cases of neurosyphilis associated with aortic disease. Fever, and even at times convulsions, may develop and these complications have been regarded as a sort of Herxheimer reaction. There are two usual methods of avoiding these occurrences. In the first place the penicillin can be preceded for two or three weeks by full amounts of oral iodide and intramuscular bismuth; or the penicillin course may be started cautiously by giving, during the first day or two, graduated amounts, i.e., a few preliminary injections of intramuscular penicillin in such small doses as 10,000 units.

Consideration needs to be given to the question of a repetition of the

ADVANCES IN THE TREATMENT OF NERVOUS DISEASES

By MACDONALD CRITCHLEY, M.D., F.R.C.P.

Neurologist, King's College Hospital; Physician, National Hospital, Queen Square.

THERE is not a great deal to report respecting neurological therapeutics within the last few years. The scope of streptomycin in tuberculous meningitis deserves, of course, a chapter to itself. Parkinsonism has been coming to the fore with the new continental remedies, parpanit and diparcol, but it would be premature to try and assess the value of these drugs. Much the same caution, if not scepticism, should be adopted towards the unfortunate publicity attending certain surgical approaches to the same disorder. Within the province of the epileptic it is now possible to write with greater experience and confidence upon the value of tridione in *petit mal*. The search for newer and better remedies in migraine still goes on but nothing of dramatic utility has yet emerged. In hypertension the cautious use of thiocyanate of potassium can be referred to with special reference to the relief of headache.

Two neurological disorders can be selected for closer discussion, namely myasthenia gravis and neurosyphilis.

MYASTHENIA GRAVIS

The older treatment with ephedrine and glycine has now given way to the following measures, employed either singly or in combination: (1) prostigmin; (2) thymectomy; (3) di-isopropyl-fluorophosphonate (D.F.P.); and (4) tetra-ethylpyrophosphate (T.E.P.P.).

For the details of the indications and contraindications for the surgical removal of the thymus the reader may be referred to the papers by Keynes (1943) and by Carson (1943). Prostigmin, however, remains the most favoured and most useful form of therapy. The present situation as regards D.F.P. and T.E.P.P. is not yet entirely beyond the domain of clinical experimentation.

D.F.P. possesses one advantage over prostigmin, namely that its action is more prolonged. The two drugs can be usefully administered together. Side-effects of D.F.P. comprise alimentary symptoms (nausea, dyspepsia, vomiting, anorexia, occasionally diarrhoea). Less often there may occur dizziness, tremors, weakness and nightmares. For particulars concerning D.F.P. the article by Comroe and his associates (1946), and the review by Quilliam (1947) may be consulted.

Burgen, Keele, and McAlpine (1948) have given a preliminary account of T.E.P.P. in the treatment of myasthenia. Again, this drug is less potent weight for weight than prostigmin, but its effects are longer lasting, and it

is also more cumulative. The central and visceral side-effects resemble those of prostigmin, and the latter can be controlled by means of atropine. Prostigmin and T.E.P.P. can be prescribed together.

PENICILLIN IN NEUROSYPHILIS

The value of penicillin therapy in cases of syphilis of the nervous system is ineluctable. But many points of uncertainty and even of dispute in this connexion still exist.

Dosage is not yet firmly established. When penicillin was first employed in neurosyphilis a course of treatment was pegged at about two million units. In subsequent reports the optimum dosage was quoted as higher, the level steadily mounting as one paper after another appeared upon the subject. The total grew from three million to four million; later still to five million and even six million. Hints of second and even third courses appeared. These shifting conceptions of penicillin therapy are somewhat disturbing and recall the initial optimism and subsequent disappointments in the early days of salvarsan. Perhaps the most common total dosage adopted to-day in the treatment of neurosyphilis is a course of five million units.

Method of administration.—The next problem concerns the manner in which this five million total is to be administered. Earlier writers suggested frequently repeated intramuscular doses of moderate size, e.g. 30,000 or 50,000 units every three hours. But later it became more usual to prescribe a single daily dose of 300,000 units for a fortnight. This latter technique obviously possesses many practical advantages if it can be shown to be as good as the older method of frequent small amounts. There is yet another mode of administration, namely to prescribe 600,000 units hourly for five days. In this case the patient needs to be in a clinic or hospital. Attempts have been made to delay the rate of absorption by using penicillin in a beeswax emulsion, but this practice has not yet come into general use. The intramuscular route remains the optimum, and intravenous injections, and continuous drip techniques have no advantages in the treatment of neurosyphilis.

Closely bound up with the details of dosage is the question of untoward *side-effects* of penicillin therapy. These are rare enough to make penicillin the treatment of choice in cases of neurosyphilis associated with aortic disease. Fever, and even at times convulsions, may develop and these complications have been regarded as a sort of Herxheimer reaction. There are two usual methods of avoiding these occurrences. In the first place the penicillin can be preceded for two or three weeks by full amounts of oral iodide and intramuscular bismuth; or the penicillin course may be started cautiously by giving, during the first day or two, graduated amounts, i.e., a few preliminary injections of intramuscular penicillin in such small doses as 10,000 units.

Consideration needs to be given to the question of a repetition of the

course after an interval. This practice is growing in favour although some writers believe it unnecessary. There is probably an interval between the conclusion of the course of penicillin and the attainment of maximum clinical and serological improvement; a delay which, according to Stokes *et al.* (1946), does not exceed four months. Purdon Martin (1948), however, believes that it is necessary to wait for a longer time before assessing results: "Of the adjuncts to penicillin the first and most important is time. Five million and six months does far more than five million alone, and in all my more recent cases I have been content to allow intervals of this order before re-examining the cerebrospinal fluid and considering the need for further therapy". Whether this Fabian attitude is justifiable cannot be asserted or denied with confidence, but some may feel that it is unsafe to allow a progressive affection like neurosyphilis to remain for months untreated, when a second course of penicillin forms a simple and safe mode of attack.

Combined therapy.—The most important and perhaps the most difficult decision concerns the use of other antisypilitic measures in association with penicillin. In dealing with general paretics the problem particularly turns on whether or not malaria therapy should be used and, if so, whether it ought to be given before, during, or after the course of penicillin. Most neurologists and venereologists favour some method of combination of malaria with penicillin, believing that the mode and rate of action of these two measures are probably different and thereby complementary. O'Leary *et al.* (1946) were among the first to compare the results of penicillin and malaria in combination. With the effects of malaria alone, according to their experience, fever therapy plus penicillin produced no better results than fever therapy alone. In this country Purdon Martin has come to the conclusion that penicillin alone is sufficient in the treatment of most cases of neurosyphilis, and that malaria is seldom called for if the patient can be kept under observation and given, if necessary, further treatment with penicillin. His plea is not altogether convincing, however, for his series of cases is a small one, and no acute instances of general paresis are included. Until a considerably greater bulk of case records are studied, and until a greater length of time has passed, we remain in ignorance about the natural history of neurosyphilitics treated with penicillin. Meantime, the wisest and at the same time most cautious plan would be to employ a combined therapy, and not to rely upon penicillin alone.

THE RESULTS OF PENICILLIN IN NEUROSYPHILIS

What type of result is to be expected after penicillin therapy? The improvement may be considered along both clinical and serological lines. Both Nicol (1948) and Worster-Drought (1947), in this country have supplied useful reviews upon the subject.

From the *clinical standpoint* an objective gain in weight may be expected, as well as a definite subjective betterment. This improvement usually appears during the actual course of injections. Even in tabetics some

lessening may occur in the frequency and intensity of pains. As might be imagined, patients with meningeal syphilis fare better than those with parenchymatous neuro-lues. O'Leary and his associates indeed thought that penicillin alone cannot control parenchymatous syphilis. The same authors point out a feature which others too have noted (and which may be significant), namely, that a few therapeutic results are outstandingly good and quite unpredictable. Another interesting and possibly important point was the one brought out by Stokes *et al.* (1946), namely, that there was surprisingly little clinical difference between the effects of low-dosage and high-dosage penicillin therapy. Purdon Martin rightly reminds us of a fact which Gowers used so often to emphasize: . . . "arrest of symptoms is all that can be expected clinically in the first instance from the most effective treatment, and it is the criterion of the effectiveness of treatment. Any positive recovery that occurs afterwards depends on the state of the nervous tissue after the disease process has been stopped . . ."

The *serological results* of penicillin medication are often striking, although Rose *et al.* (1945-1947) found no clear-cut correlation between serological and clinical betterment. As a rule the spinal fluid improves as regards cell count, protein level and the intensity of the Wassermann titres. Similar changes are, of course, to be expected after malaria therapy alone, although perhaps not so quickly. Purdon Martin found a paretic type of Lange curve continuing in an otherwise normal type of fluid. Almost all writers upon the subject of neurosyphilis pay lip service to the axiom that treatment should be aimed at the individual patient and not depend upon his mere serological reactions. Nevertheless, almost all writers immediately go on to flaunt this rule and to look to the laboratory for indices of improvement or cure, or for indications for or against further treatment. There can be no doubt that a paretic's physical or mental symptoms may persist and even deteriorate despite a steady improvement in the serological reactions. When this is the case, non-specific lines of attack may be called for, such as electro-convulsive therapy or even leucotomy, especially when there is a question of enhancement of an abnormal pre-syphilitic personality.

References

- Burgen, A. S. V., Keele, C. A., and McAlpine, D. (1948): *Lancet*, **i**, 519.
Carson, J. (1943): *Proc. Roy. Soc. Med.*, **36**, 140.
Comroe, J. H., *et al.* (1946): *Amer. J. med. Sci.*, **212**, 641.
Keynes, G. (1943): *Proc. Roy. Soc. Med.*, **36**, 142.
Martin, J. Purdon, (1948): *Brit. med. J.*, **i**, 922.
Nicol, W. D. (1948): *Post-Grad. Med. J.*, **24**, 25.
O'Leary, P. A., *et al.* (1946): *J. Amer. med. Ass.*, **130**, 698.
Quilliam, J. P. (1947): *Post-Grad. med. J.*, **23**, 280.
Rose, A. S., *et al.* (1945): *Amer. J. Syph.*, **29**, 487.
— (1947): *J. Amer. med. Ass.*, **133**, 5.
Stokes, J. H., *et al.* (1946), *Ibid.*, **131**, 1.
Worster-Drought, C. C. (1947): *Brit. med. J.*, **i**, 734.

ADVANCES IN THE TREATMENT OF DISEASES OF THE LIVER

By J. W. McNEE, D.S.O., M.D., F.R.C.P., F.R.F.P.S.

*Physician to H.M. The King in Scotland;
Regius Professor of the Practice of Medicine, University of Glasgow.*

CONSIDERABLE progress, some having a very direct bearing on clinical practice, both in medicine and surgery, can be reported since the last review of this subject in *The Practitioner* by Witts in 1945.

HEPATITIS

By 1945 much of the harvest of the war years on this aspect of hepatic disease had been gathered and collated, including the interrelations of acute infective hepatitis (epidemic and sporadic), yellow fever vaccine jaundice, "syringe jaundice" in V.D. (and other) clinics, and homologous serum jaundice. Since then some of the main developments in progress have been as follows:—

The infecting virus.—A virus is generally accepted as the cause of the above types of infective jaundice, and investigations have continued to determine whether all are due to the same virus or to different viruses. The clinical puzzle has always centred round the two incubation periods—approximately thirty day in acute epidemic infective hepatitis, in contrast to ninety days, or very often more, in homologous serum jaundice following, for instance, the administration of measles and mumps convalescent sera or any ordinary blood transfusion. In spite of much work no positive answer can yet be given. The hypothesis still remains alive that the differing incubation periods may simply be due to variations in the route of infection with the same virus, but experimental transmissions of different kinds of infective jaundice to human volunteers, both during and since the war, strongly favour the view, without giving absolute proof, that two different viruses are involved, and that infection with one does not afford protection against the other (Neefe, 1946). In medical practice second attacks of acute infective hepatitis are rare, but have been shown to occur.

Route of infection.—It has now been conclusively proved that epidemics of acute infective hepatitis can be spread by a contaminated water supply (Neefe and Stokes, 1945), and it has also been shown that in experimental transmissions to human volunteers the virus is present in the faeces during the active phase of the disease. Droplet infection from the nasopharynx and transmission by flies were both strongly suspected during the war epidemics, and a few experimental transmissions to human volunteers by nasopharyngeal washings, obtained from patients during the incubation period of the disease, have been successful (MacCallum and Bradley, 1944).

The nasopharyngeal route still seems by far the most likely common method of infection to explain the very short contact (e.g., a few hours on one day at school) noted by Pickles (1939) in his country practice.

One important clinical fact, noted during the war and strongly supported by transmission experiments, is that the main infectivity of the disease lies in the period of incubation or invasion before jaundice has appeared; hence strict isolation of an already jaundiced sufferer from acute infective hepatitis is not necessary.

Accidental transmission of infective hepatitis.—The practical problem in civil practice is now mainly concerned with the much greater use of blood transfusion as a remedy and the establishment of blood banks. When accepting donors, not only must syphilis be excluded but a question must always be asked about previous attacks of jaundice. Unfortunately, a negative history is not a complete safeguard, for, as was abundantly shown by war experiences in the large epidemics at home and abroad, a number of otherwise typical sufferers from acute infective hepatitis are never visibly jaundiced during their illness. If this is so in epidemics, when everyone is looking out for the disease, sporadic cases must often be missed in ordinary practice. The length of time the virus of infective jaundice may persist in the blood after the attack is over is unknown. The number of patients infected by transfusion of whole blood or blood constituents is already very considerable, although on the whole the actual percentage is small. It is obvious that the "pooled" blood or blood products derived from many donors at a blood bank has far greater potential infectivity than blood from a single donor. The importance of preventing accidental spread of the virus by blood transfusion must be stressed, for the recipients—many of them already in poor health—are likely to be more prone to the well-known fatal complications (acute necrosis of the liver and cirrhosis) of the naturally acquired disease. Attempts have recently been made by exposure of pooled blood or blood products to ultra-violet light (Oliphant and Hollaender, 1946) or to continuous temperatures just insufficient to injure the blood, to ensure that no virus is passed on in a transfusion, but this work is still at an early stage.

Sequelæ of infective hepatitis.—Quite apart from the sudden onset of acute necrosis (yellow atrophy) of the liver during the acute primary disease, it is now widely recognized that some patients do not recover completely but progress at various rates to the stage of chronic hepatitis or cirrhosis. A number of clinical reports are already published (Lucké, 1944; Rennie, 1945) on patients who have thus developed cirrhosis and have died of it, and much accurate pathological information concerning the gradual evolution of the cirrhosis has naturally been gained by repeated use of the technique of aspiration biopsy (Sherlock, 1948). The problem of cirrhosis seems likely to be a continuing worry for Pensions Boards, for who can say that any ex-Service man or woman who develops this disease in the coming

years did not suffer from acute infective hepatitis, without jaundice, when on war service?

The technique and use of aspiration biopsy.—This direct method of investigation of hepatic disease, originally described by Iversen and Roholm (1939) in Sweden, was developed by Dible, McMichael and Sherlock (1943) in Britain during the war epidemics and, judging by the number of publications, is now in use all over the world. Improvements in general technique and in the hollow needle employed (e.g., the Vim Silverman "split" needle in America—Kumpe *et al.*, 1947) have been made, but it must still be emphasized that the method is not free from dangers, should only be employed when full hospital facilities are available, and in medical practice (apart from research) should be restricted to cases in which all other methods have failed and accurate diagnosis is essential (Volweiler and Jones, 1947).

BIOCHEMICAL DIAGNOSTIC TESTS OF LIVER FUNCTION

Many laboratory tests continue to be employed, and it is worth noting that most recent writers suggest that a combination of several tests is essential, although not all of them recommend the same series. One diagnostic test, still in some ways empirical but thought to depend upon changes in the gamma fraction of the plasma globulin, has recently been widely used in America and is now finding acceptance elsewhere. There are really three varieties of the test—the cephalin-cholesterol flocculation test introduced by Hanger (1939), the colloidal gold precipitation test (Gray, 1940) and the thymol turbidity test developed by MacLagan in Britain in 1944. These tests have already proved of considerable value in the differential diagnosis of jaundice (Dick, 1945; Rennie, 1945). All three tend to be positive in jaundice of hepatic origin (i.e., due to actual disease of the glandular liver cells) and negative in jaundice of obstructive origin in the bile ducts. Rennie and Rae (1947), using the Hanger and Gray tests, consider the latter more satisfactory, since it is carried out with standard solutions of known chemical constitution, whereas Hanger's test makes use of a variable reagent made from sheep's brains.

PORTAL CIRRHOSIS AND NUTRITIONAL PROBLEMS IN HEPATIC DISEASE

In Britain, until the great epidemic of acute infective hepatitis during the recent war, the most common cause of cirrhosis of the liver was undoubtedly alcohol, but uncertainty always existed as to how this acted. Opinion had gradually been veering to the belief that alcohol induced chronic gastroenteritis and this in turn disturbed nutrition, the final result being portal cirrhosis as a deficiency disease. Recent important work, chiefly experimental in small animals, tends to confirm this nutritional view and requires brief discussion. The interpretation of the experiments is not easy to describe briefly since complicated problems of physiological chemistry are involved,

and those interested should consult the original papers. In 1939, György and Goldblatt, in Cleveland, U.S.A., reported hepatic injury, frequently but not invariably, in rats fed on a diet deficient in vitamin B. The injury was either a focal or diffuse necrosis, combined with fatty infiltration. The same observers continued their experiments with other dietary deficiencies (1942) and found the liver damage to be bound up essentially with the so-called lipotropic action of casein, and prevented by administration of methionine. Meantime other workers were interested in the same idea, and Glynn and Himsworth (1944) were able constantly to produce necrosis of the liver in rats by deprivation of protein alone, the diet being adequate in all other respects. Here again the addition of casein or of methionine to the diet entirely prevented the occurrence of necrosis. Best and his colleagues in Canada (1940, 1943) showed that fatty infiltration of the liver in rats can be produced by high fat diets which interfere with the nutrition of the liver cells and ultimately lead to typical Laennec's cirrhosis. The mechanism of the fatty infiltration is complex, but it also can be prevented by good biological proteins or by methionine.

All this experimental work, leading in the same general direction, naturally suggested attempts to influence human hepatic diseases, both acute and chronic, by suitable dietary measures. High protein diets, low fat diets, supplements of casein and especially of methionine have all been tried, and there are already many publications on the results.

In acute hepatic disease, especially acute infective hepatitis, casein, methionine and other amino-acids have not been found to influence greatly the course of the disease (Peters *et al.*, 1945). With regard to cirrhosis, the problem is quite different. No cure can be expected of the fixed-tissue changes present in the advanced stages of the disease, but Beams and Endicott (1947) have recently, in an important article, claimed not only great clinical benefit but remarkable histological improvement, as shown by repeated liver biopsy, in patients with cirrhosis treated energetically with methionine. The nutritional work offers much greater scope for the *prevention* of cirrhosis, both at home and abroad. It is well known that many native races living constantly on a poor diet are prone to cirrhosis, which occurs even in young children. Snapper (1941) noted in China a high incidence of cirrhosis in poor Chinese on a very low protein diet, and Gilbert and Gillman (1944) made the same observation in Bantus in South Africa who ate mainly maize and little meat. The way now seems open, when circumstances permit, for extensive clinical trials in the prevention of this probably nutritional form of cirrhosis among native races.

In Britain various changes have been made, as a direct result of the experimental work, in our dietary treatment of established cirrhosis. A diet high in protein and low in fat seemed indicated, but whilst restriction of fat has been universally accepted as important, various writers have shown that a high carbohydrate diet is even more beneficial than one rich in

protein. This confirms the long-established reputation of glucose administration in all forms of threatened hepatic failure, whatever the cause. Even the drastic reduction of fat has recently been called in question by Hoagland, Labby, Kunkel and Shank (1946), especially in acute forms of hepatitis. Two other lines of treatment in cirrhosis are at present under trial. Many clinicians have strongly supported the use of liver extracts, whilst attempts have been made to mitigate chronic reduction in plasma proteins by intravenous injection of ascitic fluid or of large doses of serum albumin.

THE RHESUS FACTOR IN DISEASES OF THE LIVER

No brief survey of this recent development in knowledge could be adequate, but the Rhesus factor is obviously concerned with some forms of hepatic disorder, especially in infancy.

SURGICAL ADVANCES IN DISEASES OF THE LIVER

As a direct result of the pioneer work of Whipple and his colleagues in America (1945), coupled with our knowledge of vitamin K and other developments in the control of hæmorrhagic states in liver disease, two important surgical advances should be mentioned:—

(1) *Operations for radical removal of carcinoma of the head of the pancreas at the ampulla of Vater.*—Various operations, one-stage and two-stage (in poor risks) have been done, and since the first of these gives the best results the difficult problem of earlier diagnosis and active treatment of painless obstructive jaundice is at once raised. Waugh and Clagett (1946) have recently reported 30 cases of radical operation with an immediate mortality of 20 per cent. The operation involves a gastric resection and removal of part of the pancreas, and is followed in many cases by steatorrhœa which is not easily controlled. The late mortality is so far undoubtedly high, and further reports are awaited.

(2) *Operations to relieve portal hypertension and portal obstruction.*—In these conditions, which affect not only chronic diseases of the liver (such as cirrhosis) but also combined diseases of the liver and spleen (especially the Banti syndrome), a common cause of death is hæmatemesis. The hæmorrhage arises either from œsophageal varices, or from rupture of large vasa brevia in the wall of the stomach, and in both instances the essential cause is portal hypertension or obstruction. Here again the new operative approach is a direct inspiration of Whipple and his school, and subsequent publications have been made, among others, by Blakemore and Lord (1945), Blalock (1947), Learmonth (1947), and Kelsey, Robertson and Giffin (1948). A good short account of the various possible operative procedures has recently been given by Learmonth. The operation is long and difficult and requires thorough team work. It consists essentially, first, in removal of the spleen followed by excision of the left kidney, the splenic vein being

joined to the stump of the left renal vein by a vitallium cannula. An alternative method is to join the splenic vein and the renal vein end-to-end without removing the kidney. The final results of this operation when successfully performed will take years to assess—the crux is whether repeated hæmatemesis will be completely prevented, and also whether no secondary changes in liver function result from the low portal pressure induced. At any rate, no permanent success has been attained by other methods in dealing with œsophageal varicose veins: the high portal pressure continues and, even when sclerosed by various methods, new varices soon occur.

OTHER ADVANCES

The syndrome of *cholangiolytic cirrhosis* has been identified by Watson and Hoffbauer (1946). This is a form of cirrhosis in which the pathological changes are small in degree and confined chiefly to the bile ducts within the liver. The disease is presumed to be an infective cholangitis, and it is suspected that at times it may be a sequel of acute infective hepatitis. It is of interest in relation to the so-called Hanot form of cirrhosis, and also because it takes us back to a jaundice and cirrhosis arising from a bile-duct infection rather than a lesion of the liver cells—a sort of intra-hepatic “catarrhal jaundice”.

A number of other advances in knowledge of hepatic diseases have been made (Snell, 1947), but the aim of this review has been to deal with advances of especial interest to the doctor in practice.

Selected References

Epidemic and other forms of Hepatitis.

Bradley, W. H. (1946): *Proc. Roy. Soc. Med.*, 39, 649.

MacCallum, F. O. (1946): *Ibid.*, 39, 655.

Memorandum prepared by Medical Officers of the Ministry of Health (1943): *Lancet*, i, 83.

Memorandum prepared by Medical Officers of the Ministry of Health (1945):

“Role of Syringes in the Transmission of Jaundice”, *Lancet*, ii, 116.

Witts, L. J. (1945): *The Practitioner*, 155, 205.

The infecting Virus.

Neeffe, J. R. (1946): *Med. Clin. N. Amer.*, 30, 407.

Route of Infection.

MacCallum, F. O., and Bradley, W. H. (1944): *Lancet*, ii, 228.

Neeffe, J. A., and Stokes, J. (1945): *J. Amer. med. Ass.*, 128, 1063.

Pickles, W. N. (1939): “Epidemiology in Country Practice”, Bristol.

Accidental transmission of Infective Hepatitis.

Oliphant, J. W., and Hollaender, A. (1946): *Pub. Hlth. Rep.*, 61, 598.

Sequelæ of Infective Hepatitis.

Lucké, B. (1944): *Amer. J. Path.*, 20, 471.

Rennie, J. B. (1945): *Amer. J. med. Sci.*, 210, 18.

Sherlock, Sheila (1948): *Lancet*, i, 817.

The Technique and use of Aspiration Biopsy.

- Dible, J. H., McMichael, J., and Sherlock, Sheila (1943): *Lancet*, ii, 402.
 Gillman, T., and Gillman, J. (1945): *S.A. J. med. Sci.*, 10, 53.
 Iversen, P., and Roholm, K. (1939): *Acta Med. Scand.*, 102, 1.
 Kumpe, C. W., Gall, E. A., Schiff, L., Molle, W. E., Safdi, S. A., and Steinberg, H. H. (1947): *Gastroenterology*, 9, 672.
 Volweiler, W., and Jones, C. M. (1947): *New Engl. J. Med.*, 237, 651.

Biochemical Diagnostic Tests of Liver Function.

- Dick, A. (1945): *Brit. med. J.*, i, 182.
 Gray, S. J. (1940): *Arch. intern. Med.*, 65, 524.
 Hanger, F. M. (1939): *J. clin. Invest.*, 18, 261.
 MacLagan, N. F. (1944): *Brit. J. exp. Path.*, 25, 234.
 Rennie, J. B., and Rae, S. L. (1947): *Brit. med. J.*, ii, 1030.

Portal Cirrhosis and Nutritional Problems in Hepatic Disease.

- Bearns, A. J., and Endicott, E. T. (1947): *Gastroenterology*, 9, 718.
 Best, C. H., and Lucas, C. C. (1943): "Vitamins and Hormones", New York.
 —, and Ridout, H. J. (1940): *J. Physiol.*, 97, 489.
 —, and Taylor, N. B. (1945): "The Physiological Basis of Medical Practice" 4th edition, London.
 Gilbert, Christine, and Gillman, J. (1944): *Science*, 99, 398.
 Glynn, L. E., and Himsworth, H. P. (1944): *J. Path. Bact.*, 56, 297.
 György, P., and Goldblatt, H. (1942): *J. exp. Med.*, 70, 185; 75, 355.
 Himsworth, H. P. (1947): "Lectures on the Liver and its Diseases", Oxford.
 Hoagland, C. L., Labby, D. H., Kunkel, H. G., and Shank, R. E. (1946): *Amer. J. Pub. Hlth.*, 36, 1287.
 Peters, R. A., Thompson, R. H. S., King, A. J., Williams, D. I., and Nicol C. S. (1945): *Quart. J. Med.*, 14, 35.
 Snapper, I. (1941): "Chinese Lessons to Western Medicine", New York.

Surgical Advances in Diseases of the Liver.

- Blakemore, A. H., and Lord, J. W. (1945): *Ann. Surg.*, 122, 476.
 Blalock, A. (1947): *Ibid.*, 125, 129.
 Kelsey Mavis P., Robertson, H. E., and Giffin, H. Z. (1948): *Proc. Mayo Clin.* 23, 195.
 Learmonth, J. R. (1947): *Ann. Roy. Coll. Surg. Engl.*, 1, 299.
 Waugh, J. M., and Clagett, O. T. (1946): *Surgery*, 20, 224.
 Whipple, A. O. (1945): *Ann. Surg.*, 122, 449.

Other Advances.

- Snell, A. M. (1947): *Quart. Bull. Northwest. Univer. med. School, Chicago*, 21, 100.
 Watson, C. J., and Hoffbauer, P. W. (1946): *Ann. intern. Med.*, 25, 195.

ADVANCES IN DERMATOLOGY

By F. F. HELLIER, O.B.E., M.D., F.R.C.P.

Dermatologist, General Infirmary, Leeds.

ANTIHISTAMINE AGENTS

THESE constitute the most important recent advance in dermatological therapy; they also are of great assistance in elucidating many problems in the morbid physiology of the skin. Wheals and possibly other reactions in the skin are caused by the local liberation of Lewis's H-substance. Attempts have been made before to counteract its histamine-like action; histamine combined with azo-protein has been injected in increasing doses in order to desensitize the body, and histaminase (torantil), an enzyme which destroys histamine, has been given by mouth. Neither of these methods has been very successful. The modern antihistamine agents act by providing a chemical group which competes with that in the histamine-like body for a receptor in the cell; in this way the H-substance is prevented from attacking the cell and exerting its action. Antihistamine agents were developed synchronously in France and America, the best known are the French antergan and neoantergan, and the American benadryl (Parke, Davis) and pyribenzamine; the last is unobtainable as yet in this country. Antergan is not used now because of its toxicity but neoantergan is available as "anthisan" (May and Baker). Another antihistamine of different formula is "antistin" (Ciba), also marketed by Boots under the name "histostab". Other substances allied to neoantergan are undergoing trials at the moment and promise to be more active and less toxic. The chief disadvantage of these bodies is their tendency to produce unpleasant side-effects.

Dosage.—The liability to develop toxic symptoms varies greatly from patient to patient and bears no relation to the therapeutic response; the latter also varies widely in different patients on the same dose. It is therefore essential to work out the correct dose for each patient, increasing it until a therapeutic effect is obtained, provided a toxic reaction is not developed first. From our investigations (Bain, Hellier and Warin, 1948) we believe that every case of urticaria can be controlled if the patient can tolerate the necessary dose. A suitable initial dose for benadryl is 50 mgm. t.d.s., and for anthisan (neoantergan) 100 mgm. t.d.s. The maximum effect of anthisan lasts longer than that of benadryl but it is usually necessary to give either drug three times a day; in those patients who develop urticaria in the early morning it may be necessary to give an extra dose last thing at night. In our experience anthisan has been more efficient and less toxic than benadryl; at times as much as 300 mgm. t.d.s. has been given without serious toxic effects, but it is unwise normally to exceed 200 mgm. b.d. A patient in bed can take a larger dose than one who is going about. The most common toxic effects are drowsiness and incoordination, headache, mild colic, diarrhoea

and nausea; the latter effect can be largely avoided by giving the tablets with food. Apparently these drugs can be given over long periods without any harm to the patient.

INDICATIONS

Urticaria.—It must be realized that antihistamine drugs are suppressive and not curative. It is still as important as ever to determine the cause of an attack of urticaria in order to prevent a relapse when the drug is stopped. In an acute attack following the ingestion of some food to which the patient is sensitive, the drugs are extremely valuable in suppressing the unpleasant symptom until the antigen has been eliminated. Unfortunately the majority of urticaria cases, at least of those which reach the dermatologist, are not due to a specific antigen but to the fact that the patient's skin is unstable and H-substance is liberated too readily in circumstances which would not affect the normal person. Such patients produce wheals when they get hot or cold, when they take violent exercise or are upset psychologically. They are benefited by antihistamine agents but often relapse when the drug is stopped. If this occurs, one is forced back on the older methods, which include a course of injections of whole blood or aolan; phenobarbitone for those in whom nervous irritability is marked, or stilbœstrol for post-menopausal cases, starting with a dose of not more than $\frac{1}{2}$ mgm. daily. Occasionally, especially in middle-aged women, a cure is obtained by giving iron and ammonium citrate, 30 grains (2 gm.) t.d.s. Papular urticaria in children also responds to antihistamine drugs but treatment should be started cautiously with a dose of not more than 25 mgm. t.d.s. for a child under five years old; on the whole children seem to tolerate these drugs well.

Eczema and dermatitis.—Reports vary greatly as to the value of antihistamine drugs in these conditions. Investigations show that they have little effect in suppressing the local lesions; this may mean that histamine plays no part in the production of these lesions, or else that the amount poured out is too large for the antihistamine drug to control. If the latter were true, better results might be expected when more active antihistamine agents are produced, but it seems more probable that histamine is not the essential feature in these reactions. The good results which have been reported may well be due to the sedative action on the central nervous system.

Pruritus.—Antihistamine drugs do at times seem to give relief in such conditions as pruritus ani and vulvæ. It is difficult to see what local action antihistamine agents can have in pruritus; there is no local whealing to suppress nor does histamine by itself cause itching; it seems more probable that here again any good effects are due to a central action. Most skin conditions have by now been treated with these drugs but the results have been of doubtful value, any improvement being due to their sedative effect. We have had some temporary success in cases of rosacea, but complete failure in ten cases of dermatitis herpetiformis; there is some evidence that they may be of value in the prevention of certain eruptions due to sunlight.

Antihistamine agents have been tried locally in pruritus ani and other

conditions. In a patient of mine with pruritus vulvæ who was sensitive to local anæsthetics, remarkable improvement was obtained with 5 per cent. benadryl in an emulsion base. Similar results have been reported by others in a proportion of cases with various pruritic dermatoses. In most of these, although there may have been symptomatic relief, there has been no objective change. These drugs are local anæsthetics, as can easily be proved by sucking a tablet; their action when used locally is probably due to this and not to any antihistamine effect. Cases of contact dermatitis due to their local application have been reported. It must therefore be concluded that they should not be used locally until all the usual treatments have been tried.

PENICILLIN

Although this is not a very recent discovery it is legitimate to assess its value now after some five years of experience. It has always been recognized by dermatologists that its sphere of action in skin diseases is limited to definite infection by sensitive organisms; local application is only of value in impetigo, impetigo (pemphigus) neonatorum, superficial folliculitis, blepharitis, and some cases of sycosis and infected eczematous and seborrhœic conditions. Parenteral injections may in addition help boils and carbuncles, some severely infected eczematous conditions, especially if there is also lymphangitis or adenitis, erysipelas and erysipeloid and occasionally grossly pustular acne. Even the above must be qualified since many cases of sycosis are due to penicillin-resistant organisms and the same is true of the other conditions. Again, sycosis is often maintained by a chronic focus of infection in the nasal sinuses and this is not affected by penicillin, either locally or parenterally. The resistance of organisms to penicillin is relative and not absolute and, *in vitro*, resistant organisms may be inhibited by high concentrations. In cases of sycosis which have failed to respond to the ordinary penicillin cream, which contains 1000 units per gm., I have had some success from using a cream containing 20,000 units per gm., or even more. This is not recommended for routine use because it is uneconomical and because of the risk of sensitization. This latter is a very real problem; in fact competent American dermatologists (Pillsbury, 1946) believe penicillin should not be used locally. It is a remarkable fact that in the early days penicillin dermatitis was rarely seen (Hellier, 1947), but it is now quite common. This may be due to a change in the penicillin itself but is more probably due to the use of penicillin in an ointment or cream instead of a sprayed-on watery solution. Many of the reactions attributed to penicillin are probably due rather to the base; this may be caused by a true sensitivity but more often is the result of a physical incompatibility. It is at all times bad to put an ointment on to an oozing surface; whatever the ointment contains it will aggravate the condition. Penicillin ointment is relatively stable and so is favoured by the pharmacists, but personally I never use it. Penicillin cream is unstable and so must be dispensed at frequent intervals and kept in a cool place but, being easily miscible with serous discharge, it

is more effective and much better tolerated by the skin. Even penicillin cream should in general not be used for more than a week, by which time all the benefit that it is likely to produce will have occurred. An exception is possibly sycosis, but even here once the skin has been cleared it is wise to change to some other application, such as quinolor ointment or eau d'Alibour. If a patient, who is having penicillin applied locally, shows any signs of increasing redness or œdema, the treatment should be stopped at once. *The indiscriminate use of penicillin applications in non-infected eczema, dermatitis or acne, or in psoriasis, cannot be too strongly condemned*; the benefit which sometimes results is due to the soothing emulsion base and not to the penicillin. Parenteral penicillin is disappointing except in acute infections like erysipelas, in which sulphonamides are equally effective.

A boil may be aborted by penicillin but it often fails to prevent further outbreaks in cases of chronic furunculosis. The primary treatment of this latter condition is sterilization of the skin by soap and water, and swabbing of all the affected areas with some mild antiseptic, together with the elimination of septic foci in the teeth or nose. Only when this has been done should penicillin be tried. Penicillin should be given in adequate but not wasteful doses. The optimum dosage is about 20,000 units four-hourly, but this is impracticable in general practice: instead, 125,000 units (1 c.cm. of the pharmacopœial preparation) in oil twice a day can be given. If the watery solution is given the dose must be 500,000 units twice a day; even this is not ideal, besides being wasteful.

RINGWORM

Much interesting research has been carried out recently on fungicidal agents. Starting from the inhibiting effect of human skin secretions on the growth of fungi, it has been shown that certain long-chain fatty acids have marked fungicidal actions; two of the most active are undecylenic and propionic acids. In clinical and laboratory tests these have proved to be among the most effective fungicides known and, in addition, they have the advantage of being practically non-irritating; the following formulæ have been used successfully by Sulzberger *et al.* (1945) and others:—

R		
	Zinc undecylenate	20
	Undecylenic acid	5
	Emulsion base	to 100

R		
	Zinc undecylenate	20
	Undecylenic acid	2
	Talc	to 100

These are now available in this country under the name of "Fungicidal Ointment and Powder" (Boots).

Many similar substances are being investigated and it is likely that the market will be flooded with them in the near future. It is, however, interesting that the classical Whitfield's ointment produces clinical results little inferior to those of the most modern fungicides.

Ringworm of the scalp has always been a difficult therapeutic problem, and in the old days cases were rarely cured until puberty, when the infection disappeared spontaneously. With the introduction of X-rays a great advance was made and it was possible to cure most cases in two to three months. The treatment could only be carried out by experts and even then was occasionally unsuccessful and not without risk of permanent loss of hair; moreover, parents often objected to a complete epilation for a small patch of ringworm. Nevertheless, it has been generally accepted that complete epilation with X-rays, or rarely with thallium, is the only satisfactory treatment for *tinea capitis*. Recently there has been a world-wide epidemic of ringworm; this, together with lack of adequate plant and staff to deal with the cases in many areas, has led to a reassessment of the whole problem. This has been aided by the use of the Wood's light, which allows much more accurate diagnosis both of cures and contacts. Ringworm of the scalp is almost always due to a small spore ringworm; this is usually a human fungus, *Microsporum audouini*, but in some instances, the proportion varying in different areas, the fungus is *M. lanosum*. This is an animal ringworm and can usually be cured by local applications alone. It would seem wise therefore, whenever possible, to identify the fungus by culture before epilating the scalp with X-rays. Attempts have been made to cure *M. audouini* infections with local treatment, using fungicides in recently discovered bases with low surface tension and high penetrating power. This has been combined with manual epilation of the infected hairs using the Wood's light. Under expert supervision a fair proportion of cases can be cured but the process takes a considerable time and is far from certain. Although in the not too distant future this method may be perfected, at the present time the treatment of choice is still epilation by X-rays.

THORIUM X

Although this is not a new form of treatment, attention has been drawn to it recently by an article by Feeny (1947) on the treatment of *alopecia areata*. He claimed to have cured 22 out of 24 cases of this condition by applying thorium X in varnish (1,500 E.S.U. per c.cm.) at monthly intervals to the bald areas. These claims should be regarded cautiously. Alopecia areata is an erratic condition and sufferers from it are often influenced by the enthusiasm of the dermatologist or the vendor of hair tonics. The essential cause of alopecia areata is psychological, and the surest road to a cure is by resolving the patient's conflicts, which are often superficial and readily exposed if the physician has time to listen sympathetically.

A patient of mine revealed after a few minutes' talk that he was "fed up" at living in his mother-in-law's house. No doubt there were deeper conflicts lurking in his subconscious, but the acquisition of a house of his own cured his depression and his alopecia.

Thorium X is of limited value in dermatology. It sometimes produces improvement in *portwine stains*, although by no means in every case. It

should be painted on about once a month for six sessions; if by then there is no change it is useless to go on, but if there has been a response a further six applications should be given. It also helps in a rare but intractable condition called *parasporiasis*. Ordinary psoriasis will respond to it, but the effect is usually only temporary.

CALCIFEROL

Following the introduction of calciferol by Charpy in France and Dowling in this country, the prognosis in lupus has been enormously improved. Many cases clear up in a matter of months on calciferol alone, but in a considerable proportion of cases local treatment and even general sunlight treatment is still necessary. Chronic scarred cases may sometimes resist all treatment. The dosage given is very large; Charpy recommends 600,000 units in the form of "sterogyl", three times a week for three weeks, then the dose is reduced to twice a week, and finally once a week for five to twelve months. I have used 100,000 to 150,000 units daily as "high potency ostelin" or in other forms.

Toxic effects.—The treatment is not without danger and it must be remembered that vitamin D₂ was used before the war in arthritis and abandoned because of its toxic effects, which included some deaths. The most common toxic symptoms are nausea and anorexia, polyuria and albuminuria, general malaise with tiredness and depression; there may be a marked increase in the blood calcium, even in the absence of symptoms, and a marked increase in the blood urea, which I have seen persist for many weeks after the calciferol has been stopped. In addition, acute "flare-ups" have been seen in patients with pulmonary tuberculosis. It is therefore a form of treatment which should only be undertaken by those with suitable experience.

Besides lupus, calciferol may benefit other forms of tuberculosis of the skin, such as *scrofuloderma*, various *tuberculides* and also *sarcoidosis*; it may cause an exacerbation of *tuberculous adenitis* followed later by improvement. Lupus erythematosus is not benefited by it. It may also help certain non-tuberculous skin conditions, including *pemphigus*, and I have seen definite improvement in two children with severe *dermatitis herpetiformis*. It has been claimed that *chilblains* can be cured by large doses of calciferol, but Anning (1947) could find no evidence of this in a considerable series of cases studied in the lupus clinic at Leeds. It is doubtful if one is justified in using such a potentially dangerous treatment in chilblains.

EMULSION BASES

Although these have now been in use for some years, they represent such a fundamental advance in dermatological technique that they must be again mentioned. In prescribing a local application it is essential to have a clear conception of what one is trying to do. When dealing with an infected oozing

lesion such as impetigo, it is necessary to prescribe an antiseptic in a vehicle which will mix with the serum. A lotion would do this or a base which is an oil in water emulsion, but a substance immiscible with water, such as soft paraffin, must not be used. If the active agent is required to penetrate the skin, as when using an anæsthetic ointment or treating ringworm of the scalp, a base with a low surface tension or one with an affinity with the skin should be used. When the skin is being irritated by some external agent, as for instance in a washerwoman's dermatitis, a protective application which is impervious to soap and water should be prescribed, and here an ordinary paste containing soft paraffin, such as Lassar's paste, is indicated.

The best known emulsifying agent producing an oil in water emulsion is "lanette wax SX". This is a mixture of high fatty alcohols, approximately 10 per cent. of which have undergone sulphonation. A suitable formula, in which penicillin or an antiseptic agent may be incorporated, is:—

R		
	Lanette wax SX	15
	Soft paraffin	15
	Water	to 100

An application containing lanette wax SX is easily emulsified with water and thus can be removed readily from the skin or the scalp; a convenient base of this type is "H.E.B. simplex". This can also be used in place of soft paraffin in pastes such as Lassar's in order to improve their absorptive action in a moist eruption.

Water in oil emulsions can be made from wool alcohols; these can be used blended with paraffins as wool alcohol ointment (B.P.), or this can be mixed with water to give hydrous ointment. This is often tolerated better by dry skins than an oil in water emulsion.

Among the most recently developed bases are the carbowaxes, a series of polyethylene glycols. Their properties vary with their molecular weight and the number of this latter is used to distinguish the different members of the series. They are freely miscible with water, and by varying the carbowax used, a preparation of the required consistency can easily be obtained.

Another new substance called "intraderm", with marked penetrating properties, has lately been introduced by MacKee and others in America. It is said to be very effective as a vehicle for sulphur compounds in the treatment of acne. Unfortunately these bases are not yet obtainable in this country, but they indicate a line along which modern dermatological therapy is making rapid advances.

References

- Anning, S. T. (1947): *Lancet*, ii, 794.
 Bain, W. A., Hellier, F. F., and Warin, R. P. (1948): (In the press).
 Feeny, P. J. (1947): *Lancet*, ii, 506.
 Hellier, F. F. (1947): *Brit. J. Derm.*, 59, 249.
 Pillsbury, D. M. (1946): *J. Amer. med. Ass.*, 132, 692.
 Sulzberger, M. B., et al. (1945): *U.S. Nav. med. Bull.*, 45, 237.

ADVANCES IN ENDOCRINOLOGY

By A. C. CROOKE, M.D.

Clinical Endocrinologist, United Birmingham Hospitals.

In this survey it is only possible to describe in detail the treatment of a limited number of endocrine diseases. It is proposed therefore to discuss those conditions in which changes have occurred recently and to omit others in which there has been little alteration.

THE PITUITARY

Acromegaly.—Treatment of the endocrinological symptoms is mainly symptomatic. Some patients appear to benefit from radiotherapy directed to the pituitary gland. It must always be remembered that neurological signs of an expanding pituitary tumour may develop at any time and require surgery, combined with radiotherapy.

Cushing's syndrome.—Patients with progressive symptoms and signs of this disease rarely respond well to radiotherapy, and the best results have been obtained with implantation of radon seeds into the pituitary gland. Treatment with various hormones has proved disappointing.

Simmonds's disease.—In the past the majority of cases diagnosed as Simmonds's disease have been suffering from anorexia nervosa and do not respond to hormone therapy. Sheehan (1939) has emphasized that Simmonds's disease is only exceptionally associated with marked wasting and then only when there are mental changes, or severe puerperal sepsis. These patients often respond well to the subcutaneous implantation of tablets of testosterone. A dose of 400 mgm. is usually sufficient to cause a marked improvement in physical condition and strength and does not cause any deleterious effects, such as the production of facial hirsuties in female patients. Its action is thought to be due to its stimulation of protein metabolism. Desoxycorticosterone may have some effect but its action is much less marked than that of testosterone. Thyroid extract is dangerous until the patient is under control with testosterone and desoxycorticosterone and its administration has resulted in death. It may, however, be given in doses of $\frac{1}{2}$ to 1 grain (32.5 to 65 mgm.) later, but its effect is often disappointing even in patients who appear to be very myxœdematous. Stilbœstrol may be given to female patients for three-weekly periods in sufficient doses to produce withdrawal bleeding, because this sometimes appears to inspire confidence and improves the mental picture. Insulin should be avoided, as these patients are very sensitive to it and readily become hypoglycæmic with minute doses.

THE SUPRARENALS

Adreno-cortical hyperactivity.—Hyperactivity may result from a tumour or

hyperplasia of the adrenal cortex. The former may be recognized clinically or by assay of the 17-ketosteroids in the urine, and requires surgery. If it is associated with the clinical picture of Cushing's syndrome the opposite adrenal is commonly atrophied, and removal of the affected adrenal results in acute adreno-cortical insufficiency, which must be treated like adrenal crisis. Contralateral atrophy is usually absent when the tumour is associated with virilism. Hyperplasia of the adrenal cortex may also be associated with Cushing's syndrome or virilism. Unilateral adrenalectomy has been tried with very variable success, and the best method of dealing with the facial hirsuties is by electrolysis. There need be no scarring if this is done with patience and at least half an inch allowed between any two hairs removed on the same day.

Adrenal crisis is a medical emergency. The patient should be treated as a case of shock: in a warm bed in a quiet secluded position. An immediate infusion of 1000 to 1,500 c.cm. of 0.9 per cent. sodium chloride and 5 to 10 per cent. glucose should be given slowly. Twenty-five c.cm. of adreno-cortical extract may be added to the infusion and 20 mgm. of desoxycorticosterone acetate in oil should also be injected subcutaneously. The infusion may be repeated every twenty-four hours until the patient is taking fluids freely by mouth. Five to 10 c.cm. of adreno-cortical extract may be given every two to four hours until he is eating well, and 5 to 10 mgm. of desoxycorticosterone daily, depending upon the blood pressure and evidence of the accumulation of excessive fluid. Crises are commonly precipitated by infections, which must be combated by active chemotherapy.

ADDISON'S DISEASE

The treatment of Addison's disease is undergoing a steady evolution. The isolation and synthesis of desoxycorticosterone by Reichstein and his co-workers in 1937 marked a further great advance, the full effect of which may be seen in the results of treatment of a series of 158 patients by Thorn and his co-workers (1942). They reported a markedly increased survival time; half of their patients were completely rehabilitated, a quarter were considerably improved, and the remainder failed to improve or died during the period of observation. Desoxycorticosterone is the only cortical steroid which is available in quantity for clinical purposes. It affects water metabolism through its control of sodium and potassium ions in the body fluids but has no effect on the other principal function of the adrenal cortex; its action on carbohydrate metabolism.

Desoxycorticosterone may be given by injection of an oily solution of its acetate ester, or by subcutaneous implantation of a solid tablet of the substance. The former is used in crises but the latter is much the best and most economical method for long-term treatment. The cortical extracts are not of much value for long-term treatment because they are bulky and expensive and it is rarely possible to give a sufficient amount for any length of time. Salt should also be given in capsules by mouth, partly because it

reduces the amount of desoxycorticosterone required and therefore reduces the cost of treatment, and partly because it acts as a safeguard against over-treatment with desoxycorticosterone (which may easily be fatal) as it can be reduced or suspended if signs of over-treatment supervene. A normal diet may be prescribed, except for a small group of patients who easily develop hypoglycæmic symptoms. These patients require frequent carbohydrate feeds. All patients must be given a fixed amount of added salt daily. Thorn recommended 1 gm. in enteric-coated capsules three times a day, because this dose can be increased up to about 20 gm. daily if the hormone therapy is found to be inadequate, or suspended if œdema develops.

The correct dose of desoxycorticosterone for an individual is difficult to determine.

Thorn recommended that each patient should be assayed separately in hospital for his daily requirements by giving him graded doses of desoxycorticosterone acetate by injection until he is stable. He then allowed 120 mgm. of desoxycorticosterone by implantation for each 1 mgm. required daily by injection. The average daily maintenance dose for his large series of patients was 4 mgm., and less than 10 per cent. of them required more than 5 mgm. daily. The principal difficulty is to determine when the patient is stable. This may be judged by his general sense of well-being and the return of his strength, weight, and blood pressure to normal. Thorn also used the ratio of the plasma sodium to potassium expressed in milliequivalents per litre. In a controlled patient this ratio should be 30; it may fall to 15 in adrenal crisis and rise to 45 with excessive treatment. The estimation of serum sodium and especially potassium is often unreliable, however, and the patient's physical condition is usually all that can be depended upon. A further difficulty is that the dose of desoxycorticosterone required to achieve stability is always larger at first than after a month or more of treatment. It is therefore necessary to keep the patient on a fixed dose by injection for a considerable time before it is safe to estimate the dose required for implantation.

In contrast to the foregoing rather complicated method of determining the dose for implantation, it is usually safe to implant 500 mgm. of desoxycorticosterone and repeat this at intervals of six to twelve months, according to the patient's condition.

The implants are best inserted through an incision in the skin of the abdomen after antiseptic preparation and infiltration with a local anæsthetic. A trocar and cannula, large enough for the tablets to pass through, is then pushed laterally for two inches beneath the skin. The trocar is withdrawn and the tablet inserted in the cannula and pushed gently to the end with the trocar, when the trocar and cannula is withdrawn. In this way several tablets can be implanted through the same skin incision radiating in different directions. It is very important that none of them should be left near the incision because they will invariably work out again. The operation is completed by placing a small thick pad of wool over the wound, and fastening it tightly in position with an adhesive bandage to prevent the tablets moving back towards the incision.

The patient must be kept under careful observation thereafter and the salt suspended at once if there are any signs of œdema or hypertension, but patients who were hypertensive before the onset of Addison's disease may become hypertensive again with adequate treatment. After a month or more when the patient appears to have regained his health he may tend to remain no longer under close observation. He will usually keep well for from six to eighteen months, when a crisis may develop rapidly and with

little or no warning. It is therefore after he has been feeling well for some months and is beginning to think he need no longer visit his doctor regularly that the danger occurs, and he should be under the closest observation.

The improvement in the results of treatment has made it possible for patients to undergo major operations. At such times they require greatly increased amounts of salt and desoxycorticosterone, as in adrenal crises. There is also an increasing number of reports of patients who have become pregnant and given birth successfully to healthy babies. They seem to tolerate pregnancy well, but require greatly increased amounts of salt and desoxycorticosterone during labour.

THE THYROID

Thyrotoxicosis.—The discovery of the *thiouracil* group of drugs has opened a new line of treatment for thyrotoxicosis but its value is still the subject of violent partisan discussion. Many authorities are opposed to its use at all, but Astwood, in his recent Addison Lecture at Guy's Hospital, considered that it should be employed in all cases. The truth must be somewhere between the two, and perhaps Peters and his colleagues (Danowski *et al.*, 1948) were nearer to it when they stated that medical treatment is the treatment of choice for elderly patients, for those with heart disease, with exophthalmos, and with hyperthyroidism recurring after thyroidectomy. The difficulty is that at present there is no way of knowing which patients are likely to relapse after an apparently adequate course of treatment.

It is not necessary to admit any but the most toxic patients to hospital and many can continue at work during treatment. Most patients need to be seen only once a week for the first month to six weeks, once a month for the next three or four months, and then every second or third month. The risk of thiouracil treatment has been exaggerated and it is sufficient that patients should be told to report immediately if they become ill. Astwood deprecated the current practice in many clinics of telling patients that the thiouracils are dangerous drugs and, as he put it, encouraging them to anticipate death three times a day. This is bound to have a deleterious effect upon the treatment of a disease in which nervous manifestations form such a prominent feature, and must surely be the reason why the thiouracil drugs have become discredited in some quarters. Agranulocytosis, which is the only cause of fatality, may develop with great rapidity and deaths have been recorded in patients whose blood was normal only two days previously. There is therefore nothing to be gained by routine examination of the blood at each visit. This unnecessary procedure has been regarded as one of the objections to medical treatment in some clinics.

A large number of anti-thyroid drugs has been tried, but *methyl thiouracil* is the one which has been used most extensively in this country and in Scandinavia, and thiourea and propyl thiouracil in America. When the thiouracil drugs were first used clinically much larger doses were employed. At present it is customary to give 50 mgm. of methyl thiouracil at four

reduces the amount of desoxycorticosterone required and therefore reduces the cost of treatment, and partly because it acts as a safeguard against over-treatment with desoxycorticosterone (which may easily be fatal) as it can be reduced or suspended if signs of over-treatment supervene. A normal diet may be prescribed, except for a small group of patients who easily develop hypoglycæmic symptoms. These patients require frequent carbohydrate feeds. All patients must be given a fixed amount of added salt daily. Thorn recommended 1 gm. in enteric-coated capsules three times a day, because this dose can be increased up to about 20 gm. daily if the hormone therapy is found to be inadequate, or suspended if œdema develops.

The correct dose of desoxycorticosterone for an individual is difficult to determine.

Thorn recommended that each patient should be assayed separately in hospital for his daily requirements by giving him graded doses of desoxycorticosterone acetate by injection until he is stable. He then allowed 120 mgm. of desoxycorticosterone by implantation for each 1 mgm. required daily by injection. The average daily maintenance dose for his large series of patients was 4 mgm., and less than 10 per cent. of them required more than 5 mgm. daily. The principal difficulty is to determine when the patient is stable. This may be judged by his general sense of well-being and the return of his strength, weight, and blood pressure to normal. Thorn also used the ratio of the plasma sodium to potassium expressed in milliequivalents per litre. In a controlled patient this ratio should be 30; it may fall to 15 in adrenal crisis and rise to 45 with excessive treatment. The estimation of serum sodium and especially potassium is often unreliable, however, and the patient's physical condition is usually all that can be depended upon. A further difficulty is that the dose of desoxycorticosterone required to achieve stability is always larger at first than after a month or more of treatment. It is therefore necessary to keep the patient on a fixed dose by injection for a considerable time before it is safe to estimate the dose required for implantation.

In contrast to the foregoing rather complicated method of determining the dose for implantation, it is usually safe to implant 500 mgm. of desoxycorticosterone and repeat this at intervals of six to twelve months, according to the patient's condition.

The implants are best inserted through an incision in the skin of the abdomen after antiseptic preparation and infiltration with a local anæsthetic. A trocar and cannula, large enough for the tablets to pass through, is then pushed laterally for two inches beneath the skin. The trocar is withdrawn and the tablet inserted in the cannula and pushed gently to the end with the trocar, when the trocar and cannula is withdrawn. In this way several tablets can be implanted through the same skin incision radiating in different directions. It is very important that none of them should be left near the incision because they will invariably work out again. The operation is completed by placing a small thick pad of wool over the wound, and fastening it tightly in position with an adhesive bandage to prevent the tablets moving back towards the incision.

The patient must be kept under careful observation thereafter and the salt suspended at once if there are any signs of œdema or hypertension, but patients who were hypertensive before the onset of Addison's disease may become hypertensive again with adequate treatment. After a month or more when the patient appears to have regained his health he may tend to remain no longer under close observation. He will usually keep well for from six to eighteen months, when a crisis may develop rapidly and with

because of the histological resemblance of treated glands to carcinoma. There has, however, been no increase of carcinoma reported in the large series of cases treated so far. This can be regarded as evidence that the thiouracils are not carcinogenic.

Iodine and thiouracil.—The administration of iodine prior to the use of the thiouracil drugs often delays the response to treatment for several weeks. It should not therefore be given until after thiouracil therapy has begun, when it has no influence on the rate of recovery. If given in this way it reduces friability of the gland, which has been reported to be a complication of thiouracil therapy making subsequent surgery more difficult.

Radio-iodine.—No large series of cases of thyrotoxicosis has yet been treated with radio-iodine in this country, but it does not appear to be entirely satisfactory. Astwood stated that the estimation of the correct dose is difficult and he therefore advised that a preliminary tracer dose should be given in order to determine what proportion is taken up by the gland. Even then some patients develop myxœdema, sometimes as long as six months later, whilst others continue to have thyrotoxic symptoms and require another dose.

Exophthalmic ophthalmoplegia.— Since the middle of the last century three types of Graves's disease have been recognized: the goitre and proptosis may appear simultaneously, the goitre may precede the proptosis, or the proptosis may precede the goitre. Pronounced cases of the latter have been called exophthalmic ophthalmoplegia by Russell Brain in this country, and hyperophthalmopathic Graves's disease by Means in America. It is a serious disease which tends to be progressive and may result in loss of the eyes. Subtotal thyroidectomy often exaggerates it, and for this reason a number of recent writers have advocated treatment with the thiouracil group of drugs when eye signs are marked. They point out that it is more easily controlled than operation and can be suspended if the eye signs get worse. Some authorities recommend giving thyroid extract with thiouracil, others have advocated œstrogens. Both are given for the purpose of depressing the pituitary gland, overactivity of which has been supposed to be responsible for the eye signs, although this has not yet been proved. In extreme cases it may be necessary to decompress the eye tissues by removal of the superior orbital plate.

DIABETES MELLITUS

The principal change in the treatment of diabetes mellitus has been in the direction of allowing more freedom in dieting. This can be achieved by controlling the carbohydrate intake and ignoring the protein and fat intake, or by controlling the total caloric intake and ignoring whether it is taken mainly as carbohydrate, protein or fat (Crooke and Scott, 1943). The latter allows a patient to have a mainly carbohydrate breakfast of, say, cereal, one morning, and a mainly protein and fat one of bacon the next. The diet is then balanced with insulin. The majority of patients are satis-

equally spaced intervals, or 100 mgm. twice in each twenty-four hours for the first month or six weeks. Thereafter the dose is reduced to a maintenance level of 50 mgm. twice or once daily, or even on alternate days. The aim should be to use the smallest dose which will produce a steady improvement in the clinical picture until normal health has been restored, with normal weight and pulse rate. Occasionally much larger doses are required to achieve this end. Treatment must be continued for at least a year after the patient's health has been restored to normal.

In almost all cases of thyrotoxicosis the basal metabolic rate can be brought back to normal by the use of the thiouracil drugs, and the general health, weight and pulse rate restored to normal in the great majority. The disappointing feature about treatment is that the disease recurs in a number of cases after cessation of treatment. The recurrence rate was much higher before it was appreciated that treatment must be continued for a considerable period of time after the patient has apparently become normal. Himsworth (1948) put the rate of apparently permanent cure at two in three of his large unselected series of patients treated for from nine to twenty-one months.

The size of the goitre is not materially influenced by thiouracil treatment unless it is given in excessive doses. The goitre then grows progressively larger. With correct dosage the goitre may ultimately diminish in size. The eye symptoms tend to subside, since the lid retraction, as measured by visible sclera above the cornea, generally subsides, but true exophthalmos, as measured by visible sclera below the cornea, may increase (Himsworth, 1948). The results of medical and surgical treatment in this respect are probably identical.

The most common toxic reactions are drug fever occurring about the tenth day after starting treatment, adenopathy, and various rashes. They are usually transitory and rarely severe. The only serious complication is agranulocytosis. It occurred in 2 per cent. of 9000 patients treated with thiouracil drugs (Moore, 1946), and 0.5 per cent. died. This series included many cases treated with the large doses in vogue in the early days of thiouracil therapy and it is believed that all toxic reactions are less common with the smaller doses at present in vogue. There is, however, no comparable review showing the incidence of complications with current low dosages. The mortality rate compares favourably with that of the best thyroid surgeons and is considerably lower than the mortality rate in most general hospitals. Agranulocytosis is not fatal in itself but becomes dangerous when infection supervenes. If a patient reports feeling ill, usually with a sore throat, it is a simple matter for any doctor to examine a smear of his blood, and if few or no granular white cells are found, penicillin should be given at once in large doses and thiouracil treatment suspended. When treatment has been started early in such cases the mortality rate is low. After recovery, thiouracil therapy should not be resumed.

Cancer has been suggested as a likely complication of thiouracil therapy

ADVANCES IN THE TREATMENT OF ALLERGY

By DAVID HARLEY, M.D., B.Sc., F.R.I.C.

Allergist to Moorfields, Westminster and Central Eye Hospital; Former Asthma Research Council Fellow and First Assistant, Allergy Clinic, Inoculation Department, St. Mary's Hospital.

ONE of the most important, and certainly the most spectacular, of recent advances in the treatment of allergy has been the introduction of the "anti-histamine" drugs, particularly as this represents the opening up of a new field of palliative treatment. Before their introduction, the main group of anti-allergic palliatives was the sympathomimetic drugs—adrenaline, ephedrine, theamin—which owed their anti-allergic action to the vaso-constrictor and antispasmodic effect which they produce: broadly speaking, a pharmacological action the reverse of that of histamine. The new anti-histamine drugs have a different action. They apparently act by blocking or preventing the action of histamine—released during the allergic reaction—analogous to the displacement of para-aminobenzoic acid by the sulphonamides.

THE ANTIHISTAMINE DRUGS

The antihistamine drugs are relatively simple synthetic substances, and those so far found effective in treatment are ethylenediamine derivatives and certain alkylamine benzyhydrl ethers, although one of the newest is an imidazoline compound. Pharmacological studies in animals have demonstrated that these substances have three main actions: (1) they alleviate bronchial constriction caused by histamine and anaphylactic shock; (2) they prevent the vasodepressor effects of histamine; and (3) they antagonize spasm of smooth muscle. Numerous experiments in animals have shown that there is a wide margin of safety between effective and toxic dosage. Another notable pharmacological action of these drugs, however, is a marked local anæsthetic effect. Possibly this may be the result of blocking the action of histamine released as part of the normal physiological process of signalling pain along the nerves. Incidentally, the antihistamine drugs have been reported to be effective in an odd variety of conditions in addition to those of frankly allergic etiology, for example, in such conditions as irradiation sickness, icteric pruritus, dysmenorrhœa, the common cold, spastic colon, and pulsating tinnitus. It is necessary therefore to avoid the pitfall of assuming that any particular condition must be allergic because it responds clinically to the administration of an antihistamine drug.

Drugs available.—The following antihistamine drugs are at present

factorily controlled with a single morning injection of globin insulin, but some tend to become easily hypoglycæmic with this. These reactions commonly occur at about the same time from one day to another in any individual, but they vary in time from one individual to another. Sometimes they can be overcome by giving more food at the meal which normally precedes them, but at others it becomes necessary to change the type of insulin. A mixture of soluble and zinc protamine insulin should be tried next and the two may be mixed together in the same syringe. It may then be found that if the patient continues to have reactions, say, at night, they can be overcome by reducing the proportion of zinc protamine to soluble insulin, or if in the morning, by increasing the proportion. Most patients seem to require a proportion of $\frac{1}{3}$ soluble to $\frac{2}{3}$ zinc protamine insulin. A very small number of patients apparently cannot be controlled by any of the slow-acting insulins and require soluble insulin three times a day.

The degree of control exercised varies from one clinic to another but an increasing number of authorities consider that glycosuria and hyperglycæmia are not in themselves deleterious. Absence of diabetic symptoms and maintenance of normal weight, together with absence of insulin reactions, constitute the principal evidence for adequate diabetic control. The patient's urinary sugar output should be kept as low as possible without his having reactions, but the amount of glycosuria which has to be allowed varies greatly from one individual to another according to how labile his blood sugar is. It fluctuates over a much wider range in some patients than in others under similar conditions, and the former are likely to show much more glycosuria than the latter when adequately controlled.

The critics who have objected to this more liberal interpretation of control have claimed that diabetic complications will develop earlier and more severely in patients who frequently show some glycosuria. This is not borne out by experience.

Dolger (1947) reviewed the arterial changes in a large series of patients in New York who had had diabetes for twenty-five years or more. He found that everyone had retinal evidence of arterial changes but that there was no difference in severity between the group which had been most carefully controlled and the group of rebels who had never consented to be properly controlled.

This evidence is very satisfactory in confirming that there is no advantage to be gained from too rigid control, but profoundly disturbing in its demonstration of our inability to deal with arterial degeneration in diabetes.

References

- Crooke, A. C., and Scott, E. (1943): *Brit. med. J.*, **i**, 64.
 Danowski, T. S., et al. (1948): *Amer. J. med. Sci.*, **215**, 123.
 Dolger, H. (1947): *J. Amer. med. Ass.*, **134**, 1289.
 Himsworth, H. P. (1948): *Brit. med. J.*, **ii**, 61.
 Moore, F. D. (1946): *J. Amer. med. Ass.*, **130**, 315.
 Sheehan, H. L. (1939): *Quart. J. Med.*, **8**, 277.
 Thorn, G. W., Dorrance, S. S., and Day, E. (1942): *Ann. intern. Med.*, **16**, 1053.

be administered with caution to patients taking the antihistamine drugs.) In certain cases, the occurrence of marked side-reactions may preclude further administration of the drug.

Some side-effects—particularly somnolence—appear to be more marked with benadryl than with antistin or anthisan, so that the choice of the preparation to be employed may be influenced to some extent by whether a sedative side-effect is desirable or should be avoided. My experience with these drugs does not afford any definite information regarding their relative indications, and by clinical trial one or other may be found superior to the other two in different cases of apparently the same clinical type, although the general impression has been gained that benadryl and anthisan are perhaps more effective in those conditions in which an extrinsic allergen of the inhalant or food type is involved, and that antistin may be more effective in certain conditions involving intrinsic and bacterial allergens, although exceptions do certainly occur.

The *indications* for the use of antihistamine drugs include: most forms of allergic œdema—acute and chronic urticaria and angioneurotic œdema, cold and heat urticaria, dermatographia, and urticarial reactions from antibiotics, insulin, liver extract, therapeutic sera, and insect bites; hay fever and extrinsic allergic rhinitis and conjunctivitis; extrinsic asthma in children; eczema and other allergic dermatoses characterized by œdema or pruritus (the results in contact dermatitis are less favourable). Good results may also be expected in a proportion of cases of certain intrinsic bacterial-sensitization conditions, such as recurrent iritis and iridocyclitis, and some forms of localized retinal œdema.

ASTHMA

In asthma in adults the results from the use of the *antihistamine drugs* have been rather disappointing. A possible explanation of this, recently suggested by Dale, is that there may be two types of histamine action in allergic conditions, namely “extrinsic” and “intrinsic”, depending upon whether the released histamine (a) produces its action on tissues external to that in which the histamine is released (for example, the release of histamine from the nasal mucosa in hay fever acting on the neighbouring capillaries and producing œdema), or (b) acts on the same tissue in which the release takes place. Dale cites asthma as a probable example of this intrinsic type—the histamine being released from, and acting upon, the bronchial muscle—and suggests that the antihistamine drugs may be effective in the extrinsic type but not in the intrinsic type, although this does not explain why the drugs are often beneficial in asthma occurring in children. Another factor which may have a bearing on the problem is the infective or bacterial element in asthma, which is shown by clinical experience to be of etiological importance in many cases of asthma in adults.

Adrenaline substances.—As palliatives for oral administration it is now

generally available in this country:—

Benadryl (Parke, Davis) (β -dimethylaminoethyl-benzhydryl-ether).

Anthisan (May and Baker) (*p*-methoxybenzyl-pyridyl-dimethylethylene-diamine).

Antistin (Ciba) (2[phenyl-benzyl-aminomethyl]-imidazoline).

For therapeutic purposes the hydrochloride or other salt of the above bases is used. They are put up in tablet or capsule form for oral administration (50 or 100 mgm.) and in solution for parenteral injection. Benadryl is also available in elixir form (10 mgm. in 4 c.cm.).

Dosage.—The average adult dose is 50 to 100 mgm. by mouth three or four times daily, preferably administered after meals and at bedtime. In severe cases, acute or chronic, this dosage may be inadequate to achieve satisfactory symptomatic control. In these cases, as much as 300 to 400 mgm. or more per day, in doses of 50 or 100 mgm., may be required during the initial period of treatment. In acute cases the patient should be instructed to await the effect of the initial dose for at least two hours before a further dose is considered. In this type of case the treatment may be started with the average dosage of 50 to 100 mgm. three to four times daily, and the total dose is increased by 50 to 100 mgm. each day until satisfactory results are achieved. A dosage of 400 to 600 mgm. per day must be regarded as the maximum. When partial or complete relief is obtained, the dosage can usually be cut down and a maintenance dose of 100 to 150 mgm. per day is often sufficient to prevent recurrences. In all cases the optimal daily dosage must be determined by clinical trial. In conditions such as pruritus, which are usually more disturbing at night, the bedtime dose may be increased and the daytime dosage reduced. Infants and children may be treated on the basis of body weight; the average daily dose varies from 20 to 100 mgm.

Generally speaking, in acute cases the response to the drug is prompt. If no effect is noted within three hours the dosage may be inadequate. If a trial of increased dosage over a period of twelve to twenty-four hours does not show reasonably satisfactory control of symptoms, the treatment must be considered unsuitable. In milder and more chronic conditions, when a low daily dosage is being administered, a longer trial period may be necessary.

Parenteral injection should be reserved for the initial treatment of acute attacks, or when oral treatment is impracticable or insufficient. A dosage of 50 to 100 mgm. by the subcutaneous, intramuscular, or slow intravenous route may be used. Usually about 3 injections in twenty-four hours is regarded as the maximum. One or two cases of severe reaction to parenteral therapy have been reported, so it should not be used indiscriminately; similarly, the possibility of some oxytocic action calls for caution in administration of the drugs to pregnant women, until further information is available.

The most common *side-effects* are drowsiness, dizziness, nervousness, lassitude, nausea, and dry mouth; occasionally more severe reactions occur. Such reactions do not always bear a direct relationship to the size of the dose administered, although many patients who experience these side-reactions initially may be well able to continue the treatment on reduced dosage. Gastric discomfort may be reduced to the minimum by taking the drug immediately following a meal or with a glass of milk and a biscuit. Mild sedative effects are not altogether undesirable in many patients, particularly following a night-time dose of the drug, but when such effects become more severe, especially during the daytime, measures for their relief may be desirable. The administration of caffeine, ephedrine, or small doses of benzedrine, is often sufficient to prevent or alleviate these reactions. (In view of these sedative effects, it must be noted that hypnotics and sedatives, particularly the barbiturates and opium derivatives, should only

I employ the term "*bacterial-sensitization*" for all those cases of allergic disease in which the allergen originates from an infective focus, which may be either at the site of the allergic response (as respiratory tract infections may produce asthma or rhinitis) or at a distance from it and be conveyed to the shock tissue usually by the hæmatogenous route (as a peridental infection may produce urticaria, or a tonsillar infection may produce iridocyclitis). The term also includes those cases of allergy to extrinsic allergens in which the specific allergen tolerance is lowered by an infective process; e.g., in Koenigsfeld's example of asthmatic attacks induced by amidopyrine only during the course of an intestinal infection; and in Urbach's case of a woman who had an extensive phlegmon on one leg and in whom the oral administration of quinine produced an exanthem confined to the previously infected area. Although clinical experience of specific treatment in allergic manifestations produced by bacterial-sensitization gives considerable support to the hypothesis that the relationship between the infective process on the one hand and the allergic manifestation on the other is one of cause and effect, it must be admitted that the precise nature of the mechanism involved is by no means clear at present. Furthermore, the use of skin tests with bacterial vaccines and extracts has proved relatively unsatisfactory as a diagnostic measure, particularly in the asthma group, in sharp contrast to the reactions obtained with extrinsic allergens in inhalant and food sensitizations.

In my opinion, many cases of so-called *food-sensitization allergy*, in which the attacks are definitely referable to the consumption of a particular food and are reduced or cease when that food is withheld, but in which the skin reaction to the food is negative, are due to the effect of the food on an established intestinal infection leading to increased production of bacterial allergens which activate a bacterial-sensitization mechanism. In these cases the urticaria or asthma or other manifestation does not usually develop until eighteen to twenty-four hours after the consumption of the suspected food, in contrast to the shorter period between consumption and onset of symptoms in a true food sensitization.

The older theory of *bacterial toxæmia* or a *toxic focus* which was based on the conception of a primarily toxic action of bacterial products elaborated in the focus, was found to be untenable in the majority of cases of these conditions classified by me as bacterial-sensitization, although it is admitted that proven instances of such a mechanism have occasionally been recorded. If the matter be considered from the standpoint of allergy, and if the processes involved be regarded as an allergic sensitization to bacterial products, and not as a primarily toxic effect, many of the objections to the older bacterial toxæmia theory are removed. The chief objections to the bacterial toxæmia theory were, first, the failure to achieve good results by surgical means in the majority of cases in which a localized focus, capable of removal, was found, and secondly, the failure to find an infective focus at all in many cases.

The main reason for the relative failure of surgery in such cases is probably an immunological one. If in fact the mechanism were one of primary toxic action—usually considered to be a fairly specific process—such failure would have been a serious objection to the theory of bacterial sensitization. But if the mechanism be regarded as an allergic reaction to the nucleo-protein or to an endotoxin of the organisms concerned, the matter takes on a dif-

generally recognized that combinations of ephedrine, theophylline, and a sedative, are superior to either ephedrine or theophylline alone, and the judicious use of such preparations will greatly diminish the need for regular palliative injections of adrenaline, or recourse to adrenaline-containing inhalants, in chronic asthma, and will thus allow of the latter to be kept in reserve for emergency use. The following are the two preparations of this type which I find most useful:—

Tab. Franol (Bayer): ephedrine $\frac{3}{20}$ grain (10 mgm.), theophylline 2 grains (0.13 gm.), luminal $\frac{1}{2}$ grain (8 mgm.).

Pulvules Amesec (Lilly): ephedrine $\frac{3}{8}$ grain (25 mgm.), aminophylline 2 grains (0.13 gm.), amytal $\frac{3}{8}$ grain (25 mgm.).

RHINITIS

For local administration in allergic rhinitis of the bacterial-sensitization type, Antistin-Privine (Ciba) is often very effective, although for all types of extrinsic allergic rhinitis and conjunctivitis I think there is nothing to equal the old-fashioned weak adrenaline and cocaine drops, provided they are carefully compounded:—

R Adrenaline chloride (1:100 solution, Parke, Davis) . . contents of one 10 c.cm. bottle
Cocaine hydrochloride 2 grains (0.13 gm.)
Boric acid 30 grains (2 gm.)
Distilled water to 2 ounces (57 c.cm.)

To be made up in the form of drops—2 or 3 drops in each nostril and/or eye occasionally. Do not use after three months.

(The wording of the instructions about the adrenaline is to ensure that a fresh and potent solution is used.)

Although all palliatives have their place in the treatment of allergic conditions, and may be valuable preliminaries or adjuncts to more specific lines of treatment, it must be borne in mind that the regular and continued use of any palliative treatment, no matter how successful, is essentially a confession of failure to succeed with a more rational and specific therapy.

BACTERIAL INFECTION IN ALLERGIC CONDITIONS

“The rôle played by micro-organisms in calling forth the basic mechanisms of allergization cannot be overestimated” (Urbach, 1946)—thus the considered opinion of one of the world’s leading authorities. This is an aspect of the subject which seldom receives the attention it undoubtedly merits, but which is of great importance in treatment. One of the main reasons for this relative lack of attention has been generally the preoccupation of many allergists with skin testing to extrinsic allergens, and particularly the indiscriminate use of the intradermal method of skin testing, which commonly produces false positive reactions. On the other hand the adequate investigation of the infective factor in allergy patients is a much more difficult and complicated business.

ADVANCES IN OTOTOLOGY

By GEOFFREY BATEMAN, B.M., F.R.C.S.

Assistant Surgeon, Ear, Nose and Throat Department, St. Thomas's Hospital.

SECRETORY OTITIS MEDIA

This condition has attracted more attention since it was discussed by Gordon Hoople at the Royal Society of Medicine in February 1944. It is much more common than was generally supposed and any otologist who is actively looking for it finds it in patients of all ages.

The condition consists of a clear effusion into the middle ear causing a conduction deafness. The patient complains of deafness which comes on fairly suddenly, and can usually name the day on which he became deaf. Frequently the complaint is not of deafness but of a muffled feeling in the ear which to the observer would seem to be the same thing. The patient, however, is emphatic that he is not deaf but that his ear is muffled. Otherwise there is often no other aural symptom, although occasionally there is a short bout of minor earache. I have seen one patient who had severe earache for several hours followed by a copious discharge for about an hour, and since then no pain and no discharge, but a deafness which persisted for several weeks until treated. The deafness is usually first noticed towards the end of a nasal infection and may be a complication of vasomotor rhinitis or nasal allergy.

The *cause* of the condition is unknown. The fluid is stringy and clearly has a mucous content. It is sterile and no organisms can be seen in it on microscopical examination. There is usually a low cell count, mainly lymphocytes, in the fluid. As it is often a sequel of a nasal infection, it is likely to be infective and the absence of demonstrable organisms suggests the possibility of its being due to a virus infection. Another possibility is that it is an allergic reaction. If this were so a high eosinophil count in the fluid might be expected, but this has not been demonstrated.

Diagnosis.—To make the diagnosis the surgeon must actively look for the condition in any case of conductive deafness of sudden onset which does not show obvious signs of active otitis media. The diagnosis rarely comes to the passive examiner of ears. Hence the comparative rarity with which the diagnosis is made.

There is a type with black or blue drum which is very obvious and quite rare. This diagnoses itself and need not be further discussed, although it is often thought to be a hæmotympanum on account of its appearance.

The ordinary type is less easy and at first glance presents a normal tympanic membrane. However, on close examination the membrane will be seen to be somewhat waxy in appearance and rather dark, so that the

ferent complexions. Bacterial nucleo-proteins are not type-specific (those of the pneumococci and viridans streptococci are not even strictly species-specific) so that a considerable degree of immunological overlap exists. Now when dealing with those species of organisms which commonly inhabit man, both as commensals and pathogens, it does not follow because, say, a streptococcal focus in the tonsils is removed, that the supply of nucleo-protein allergen to the site of the allergic reaction is completely cut off, because other types of streptococci with similar nucleo-protein may be present in other parts of the body, and may be able to keep the reaction going. The problem therefore would seem primarily to be one that calls for an attempt to change the patient's abnormal reactions to those of normality.

Although the surgical removal of a focus may be a desirable thing, it should not for the foregoing reasons be usually more than secondary to appropriate desensitization treatment. Indeed in some instances surgery is definitely inadvisable as the first step in treatment; a well-known example being the frequency with which asthma follows radical surgical operations on the allergic nose when preliminary desensitization is omitted.

The second objection to the bacterial toxæmia theory, namely the failure to find a toxic focus, should be regarded as primarily a matter for the bacteriologist, since a toxic focus does not necessarily entail the presence of diseased tissue, or of clinical signs of an acute or chronic infection, and accordingly ordinary clinical diagnostic methods are likely to be inadequate, although it is not suggested that the latter should be omitted as a routine measure.

In the case of allergic sensitization to inhalants, foods and the like, it is possible to resort to the skin test, but in bacterial-sensitization the use of bacterial vaccines, extracts and solutions for skin tests has proved relatively unsuccessful. Fortunately, another technique is available for tackling the problem from a different angle. This is the method of *pathogen-selective culture*, otherwise known as the Cohen-Heist technique. The principle of the method is the utilization of the *in vitro* bactericidal power of the patient's whole fresh blood to kill off organisms to which the patient is "immune" and to allow the growth of potential "pathogens". In my experience, this method for the detection of toxic foci and for the preparation of bacterial antigens for therapeutic desensitization is extremely valuable, and would appear to be the only rational method at present available.

CONCLUSION

It must be emphasized that in the main the successful treatment of the allergic diseases still depends upon the accurate assessment of the various specific causal factors operating in the individual patient, and that no universal or non-specific cure, or other short-cut to success in the treatment of allergic conditions, is as yet materializing.

The perforation seals up with serum in a few minutes and, unless it is made through an old thin cicatrix, it will be firmly and soundly healed in a couple of days.

The middle ear may refill with fluid, in which case the procedure must be repeated. This is not usual.

In small children the condition is usually cured by removal of the obstructing adenoids, but radiotherapy to the Eustachian tube may occasionally be necessary. If this fails the membrane is incised and the Eustachian tube catheterized under general anæsthesia. Unfortunately this may on occasion have to be repeated, although this is rare. It might be thought that this would be a dangerous procedure and likely to cause an infective otitis media. It is not my experience that this is so. I have not yet seen an acute otitis media caused by incision and inflation in this way.

It seems probable that many cases of deafness due to dry middle-ear catarrh are in fact the end-result of untreated secretory otitis, and for this reason alone the condition should be emphasized and the possibilities of cure publicized. Secretory otitis may be grouped with impacted wax as conditions in which the patient can come to see the doctor a deaf man and leave a few minutes later with normal hearing.

MÉNIÈRE'S DISEASE

The interest in Ménière's disease was stimulated by the publication of the paper by Hallpike and Cairns (1938) on the pathology of the condition. It is now generally accepted that the essential lesion is hydrops of the endolymphatic system.

The surgery of the disease is still developing and a number of different operations are performed. All surgical procedures aim at destruction of the function of the affected labyrinth. It is well known that a patient can rapidly compensate for the destruction of one labyrinth and in a few weeks his remaining labyrinth will regulate equilibration very efficiently, and most subjects will suffer no lasting disability. However, the destructive operations have this serious defect, that it is not always possible to diagnose which labyrinth is causing the attacks of vertigo. Furthermore, the second labyrinth is sometimes affected by the disease and bilateral labyrinthectomy does cause a serious and lasting disability. In addition, most operations destroy the hearing in the ear subjected to operation, with the result that bilateral labyrinthectomy usually leads to total deafness.

The operations performed to-day, with their advantages and disadvantages, are:—

(1) *Transmastoid labyrinthotomy* with injection of alcohol into the perilymphatic system is still a popular operation. It is safe and easy and without danger to the patient. It always destroys the hearing.

(2) *Wright's operation* of injecting alcohol by passing a needle through the tympanic membrane and the footplate of the stapes, has the advantage of involving no open wound and therefore invalidism is minimized. It is rarely done now as several cases of facial palsy have been reported as complicating the operation. It also destroys the hearing.

examiner wants to adjust his light or blames the battery of his otoscope. There may be a hairline where the fluid and air meet in a part-filled middle ear. This is always concave upwards and the handle of the malleus divides the line into two halves, both concave upwards. The position of the hairline will change with the position of the patient's head and with examination with a pneumatic speculum. Bubbles may be seen in the middle ear scattered over the tympanic membrane and the position of these will change with examination with the pneumatic speculum. They look like irregularly disposed translucencies in the texture of the membrane.

The Eustachian tube is often patent to Valsalva's manœuvre and this in no way invalidates the diagnosis; but it gives useful information. Normally after auto-inflation the membrane returns to its normal position reasonably slowly. With secretory otitis the membrane snaps back into position as though it were elastic. This is a striking sign if it is looked for. Very occasionally auto-inflation froths the fluid into bubbles and makes the diagnosis easy. The membrane should always be watched while the patient is auto-inflating, as it is the movements of the membrane which lead to the diagnosis in many cases, rather than the appearance after auto-inflation.

Eustachian catheterization may help in the diagnosis and should be done in cases of doubt. The sound of the passage of air is clear and loud so that at first the surgeon thinks it is normal. But it is unusually clear and loud and it has a harsh quality, and I am told that with practice the sound is characteristic. I cannot claim to recognize the peculiar qualities of the sound but its very normality in a deaf person, its clearness and loudness have often led me to a correct diagnosis.

Incidence.—Secretory otitis is common in children with large tonsils and adenoids; surprisingly common when it is actively looked for. It is also common in young adults and adults after colds and influenza. It is seen also in the aged with their running noses and rheumy eyes. The deafness of the aged which has suddenly increased should not be dismissed as presbycusis until secretory otitis has been excluded, for, of course, the two conditions can and do coexist.

Flying can cause an indistinguishable condition, and acute otitic barotrauma settles down into a secretory otitis which is the usual cause of persistent deafness after a barotrauma.

Treatment.—The treatment is evacuation of the fluid. This is best done by making a small incision through the tympanic membrane and blowing the fluid through the perforation by inflation of the Eustachian tube. This inflation can be done by repeated auto-inflation or by Eustachian catheterization. No anæsthetic is needed for the incision of the membrane.

A small incision, no more than a large prick, is made low down in the posterior segment midway between the umbo and the periphery of the membrane. A pneumatic speculum then demonstrates the fluid. The Eustachian tube is inflated and a stream of fluid comes through the perforation and collects in the meatus. This is mopped out and inflation repeated until only air whistles through the perforation.

The perforation seals up with serum in a few minutes and, unless it is made through an old thin cicatrix, it will be firmly and soundly healed in a couple of days.

The middle ear may refill with fluid, in which case the procedure must be repeated. This is not usual.

In small children the condition is usually cured by removal of the obstructing adenoids, but radiotherapy to the Eustachian tube may occasionally be necessary. If this fails the membrane is incised and the Eustachian tube catheterized under general anæsthesia. Unfortunately this may on occasion have to be repeated, although this is rare. It might be thought that this would be a dangerous procedure and likely to cause an infective otitis media. It is not my experience that this is so. I have not yet seen an acute otitis media caused by incision and inflation in this way.

It seems probable that many cases of deafness due to dry middle-ear catarrh are in fact the end-result of untreated secretory otitis, and for this reason alone the condition should be emphasized and the possibilities of cure publicized. Secretory otitis may be grouped with impacted wax as conditions in which the patient can come to see the doctor a deaf man and leave a few minutes later with normal hearing.

MÉNIÈRE'S DISEASE

The interest in Ménière's disease was stimulated by the publication of the paper by Hallpike and Cairns (1938) on the pathology of the condition. It is now generally accepted that the essential lesion is hydrops of the endolymphatic system.

The surgery of the disease is still developing and a number of different operations are performed. All surgical procedures aim at destruction of the function of the affected labyrinth. It is well known that a patient can rapidly compensate for the destruction of one labyrinth and in a few weeks his remaining labyrinth will regulate equilibration very efficiently, and most subjects will suffer no lasting disability. However, the destructive operations have this serious defect, that it is not always possible to diagnose which labyrinth is causing the attacks of vertigo. Furthermore, the second labyrinth is sometimes affected by the disease and bilateral labyrinthectomy does cause a serious and lasting disability. In addition, most operations destroy the hearing in the ear subjected to operation, with the result that bilateral labyrinthectomy usually leads to total deafness.

The operations performed to-day, with their advantages and disadvantages, are:—

(1) *Transmastoid labyrinthotomy* with injection of alcohol into the perilymphatic system is still a popular operation. It is safe and easy and without danger to the patient. It always destroys the hearing.

(2) *Wright's operation* of injecting alcohol by passing a needle through the tympanic membrane and the footplate of the stapes, has the advantage of involving no open wound and therefore invalidism is minimized. It is rarely done now as several cases of facial palsy have been reported as complicating the operation. It also destroys the hearing.

(3) *Cawthorne's* (1943) operation of opening the external semicircular canal and removing the membranous external canal is effective in destroying the function of the labyrinth and has in some cases preserved the hearing. It is not widely practised, perhaps because it is much less simple than the frankly destructive operations and its advantages have not been fully substantiated.

(4) Recently Day (1946) of Pittsburgh has recommended *diathermy of the vestibule* as a means of destroying the labyrinth without destroying the hearing. He opens the external canal with a transmastoid approach and threads a fine diathermy needle through this opening forwards into the vestibule. The current is then switched on and kept on for a second or two until the perilymph bubbles. The face often twitches when the current is on and there have been several cases of facial palsy. However, there have been cases in which the hearing has been fully preserved and the labyrinth effectively destroyed.

(5) Finally, *section of the vestibular portion of the 8th nerve*, popularized by Dandy, is still performed. As it is a major intracranial operation, however, carrying a small mortality, it is not very popular.

The *medical treatment* has also received much attention and some of the results are promising. Miles Atkinson (1945) has emphasized the vascular theory of the causation of the disease. He divides the cases into a primary vasodilator group and a primary vasoconstrictor group, distinguishing the groups by a histamine skin test on the flexor aspect of the forearm. The primary vasodilator cases he treats by *histamine desensitization*, and the primary vasoconstrictor cases by ingestion, and perhaps injection, of *nicotinic acid*. This drug is used for its vasodilator effect and not as a vitamin. Large doses must be employed: 100 mgm. three times a day is an average starting dose. The results of this treatment are most encouraging.

Fowler and Glorig (1947) have suggested using the toxic effects of *streptomycin* on the eighth nerve in the treatment of the disease. Streptomycin seems to have a selective toxic effect on the eighth nerve and has a greater effect on the vestibular division than on the auditory division. They have succeeded in several cases in depressing the vestibular function sufficiently to cure the symptoms without affecting the hearing. This slow labyrinthine destruction does not cause the violent vertigo which is caused by operative destruction. However, both labyrinths are equally affected and cure therefore results in total suppression of labyrinthine function, which is a serious handicap in the dark.

FENESTRATION FOR CLINICAL OTOSCLEROSIS

During the post-war years the fenestration operation for clinical otosclerosis has become established in this country and many surgeons are performing it. The indications for the operation are gradually being worked out and with each surgeon's increasing experience results are becoming better. There seems little doubt that the operation is now a reasonable procedure for any otosclerotic individual who shows no serious loss of cochlear function as he will have at least a fifty per cent. chance of getting lasting restoration of useful hearing. The fate of the failures is an important factor in advising patients about the operation. There is always some deformity of the meatal wall so that most patients will require removal of wax from the cavity at six-monthly intervals. Occasionally there may be persistent otorrhœa,

although this is unusual. The hearing after a failure usually returns to its preoperative level and after this the course of the deafness proceeds unaltered by the operation. Rarely the hearing is seriously depressed. This is due to some affection of the labyrinth during the postoperative period, the escape of blood into the perilymphatic space, or damage to the membranous labyrinth during the operation, or rarely to infection of the labyrinth. However, any serious depression of the hearing by the operation is rare and all but about five per cent. of cases show immediate improvement of the hearing.

Facial palsy is a possible complication but a permanent palsy is very rare and should not occur except in most exceptional circumstances. The risks to life are extremely slight in the fenestration operation, and these risks are entirely anæsthetic risks.

MASTOID SURGERY

The fenestration operation has improved mastoid surgery and undoubtedly this meticulous temporal bone surgery will ultimately raise the general level of mastoid surgery. In the past, radical mastoid cavities often remained moist and the Eustachian tube was blamed. In the light of present knowledge some of these cases are recognized as being due to infection in the hypotympanic cells and to be curable by suitable surgery. The fenestration operation demands hæmostasis; this can also be obtained in radical mastoid surgery. With adequate hæmostasis the structures of the middle ear can be seen and disease dealt with without risk to the facial nerve, the footplate of the stapes and other vital structures. This has resulted in a realization that persistent otorrhœa after radical mastoid surgery is usually due to a defect in the technique of operation and in many cases is not an inevitable sequel.

PENICILLIN IN ACUTE OTITIS MEDIA

The status of penicillin in the treatment of acute otitis media and its complications will be a source of argument for many years. The present position may be summarized by these short statements:—

(1) Penicillin in adequate dosage has reduced the mortality of acute otitis media and its complications to a negligible figure.

(2) Penicillin has not replaced surgery in acute infective ear diseases but it has rendered surgery safe, and has enabled the surgeon safely to delay operation and thus to avoid operation in some cases.

(3) Relapses after improvement under penicillin therapy are reasonably common and patients must therefore be kept under close observation until all symptoms and signs have resolved.

It should be emphasized that penicillin, like sulphonamide therapy, does not cure all cases of acute otitis media even though given early and in infection with penicillin-sensitive organisms. It is not therefore sufficient to administer penicillin and assume that the ear will become well. Many articles have been published on this subject, but the well-known difficulty

of assessing the effect of treatment in acute otitis media, usually a self-limiting disease, makes evaluation very difficult, and only further experience will finally solve this problem.

THE NATIONAL HEARING AID

This is an electric hearing aid developed by a subcommittee of the Medical Research Council. The Ministry of Health has ordered large numbers of this instrument, and with the introduction of the National Health Service on July 5, 1948, this aid will now be issued free to all deaf persons to whom it is recommended by an otologist. The Ministry of Health proposes to set up hearing aid centres at all big hospitals, to be under the supervision of the otological staff of the hospital, and it is through these centres that the hearing aids will be issued and serviced. This is clearly an enormous undertaking, for although estimates of the number of deaf persons in the country vary enormously it seems likely that something of the order of 400,000 persons will eventually be recommended for the hearing aid. These hearing aid centres will take some months, or even years, to get into full operation, and at first the supply of aids is likely to be limited, so that practitioners are advised not to rush their patients to hospital during the first few months of operation of the scheme.

The use of a hearing aid is an acquired facility and is not instinctive. Patients will therefore need encouragement to ensure that they persist in using the aids until they get full benefit from their use. Ultimately it seems likely that instruction classes will be incorporated in the hearing aid centres, and when this has come about the centres will supervise the patients for some time after the issue of an aid. At first, however, these facilities will not be generally available and the practitioner will undoubtedly be consulted by patients about the use of an aid. The patient must become accustomed to a noisy environment before he can distinguish speech coming through this noisy background. This is just the position of a countryman trying to converse in a busy city street. He is confused by the noise and hastens back to the peace of the country. So it is easier for the deaf person to hear a shout without the aid than a conversational voice with the aid until he has become accustomed to the noisy environment. The practitioner should therefore encourage his patient to persevere with his aid until he is accustomed to the noise and can distinguish speech through the noisy background. A recent article by Scott Stevenson (1948) is most instructive on this subject.

References

- Atkinson, E. M. (1945): *Arch. Otolaryng.*, Chicago, 42, 186.
 Cawthorne, T. (1943): *J. Laryng. Otol.*, 53, 363.
 Day, K. M. (1946): *Laryngoscope*, 53, 33.
 Fowler, E. P., Jun., and Glorig, A. (1947): *Ann. Oto.-rhino.-laryng.*, 56, 379.
 Hoople, Gordon, D., and Blaisdell, Irl H. (1944): *Proc. Roy. Soc. Med.*, 37, 270.
 Hallpike, C. S., and Cairns, H. (1938): *J. Laryng.*, 53, 625.
 Stevenson, R. Scott (1948): *Brit. Med. J.*, i, 990.

ADVANCES IN OPHTHALMOLOGY

By IDA MANN, D.Sc., M.B., F.R.C.S.

Surgeon, Moorfields, Westminster and Central Eye Hospital.

The post-war years have entailed for all specialties, including ophthalmology, much reconstruction and re-orientation in the attempt to return to normality. During the war such energy as could be spared for original work was naturally directed into channels of research intimately connected with war needs, and much of such work was of necessity at the time, secret. It follows therefore that although post-war advances in the subject are not outstanding, yet the post-war ophthalmic literature, dealing mainly with war-time observations, contains much that is suggestive and new. Both British and American literature reflect this trend. Switzerland, on the other hand, has, during her period of isolation, produced the essentials of a new method of diagnosis, highly technical and academic at present, but wholly unconnected with war and rich in possibilities of future discoveries in ophthalmic pathology. Some of this recent work can be described under the headings of clinical, therapeutic, diagnostic and academic advances.

CLINICAL ADVANCES

In the clinical field we find attention focused on *nutritional disease*, through the work of those connected with prisoners of war. Here, although the amount of material is vast and the clinical observations numerous, yet the lack of facilities for the scientific working out of the problem has so far prevented a full understanding of many of the conditions met with. Nutritional amblyopia is a new disease so far as England is concerned, although it has been known and described in the tropics for some time. A study of the symposium on the subject held at the meeting of the Ophthalmic Society of the United Kingdom in 1947 will show how complex is the problem. All observers agree that the disease shows essentially an amblyopia from a small central or paracentral scotoma with retention of the peripheral field, together with other general signs of malnutrition. There is a similarity to other forms of retrobulbar neuritis, for example, that found in disseminated sclerosis, but the nutritional type tends to produce permanent damage, irreversible by any of the known vitamins. That the B complex is implicated seems likely, but some other factor, probably a protein deficiency, must also be present in the diet.

Other nutritional diseases of the eye, e.g., those due to lack of a single vitamin (Wolbach and Bessey, 1942; Mann *et al.*, 1946), have also been studied during the war, both experimentally and clinically, and knowledge, especially of deficiency of vitamin A and vitamin B₂, has been extended.

It is interesting to note that extreme depletion of vitamin A (extending in adults over months or years) must occur before any ocular signs are detectable, the eye, as it were, holding on to the stored vitamins longer than most other tissues.

Another advance, perhaps less directly due to the war, has been in the field of ocular symptoms in *endocrine diseases*. It was noted by many physicians and ophthalmologists that cases of extreme exophthalmos following thyroidectomy, or associated with a low basal metabolic rate (Mann, 1946), appeared to be increasing in frequency during the "blitz." The problem was attacked from many angles, and although there is still much need for research, we now have a better idea of the relative rôles of the thyrotrophic hormone of the pituitary, of thyroxin, of the gonads and of the hypothalamus in the production of the different types of exophthalmos, lid œdema, ophthalmoplegia and lid retraction found in complicated cases of endocrine imbalance (Pochin, 1944; Mann, 1946). This has led to modifications in treatment, since certain cases of exophthalmos improve under treatment with thyroid extract and others with testosterone, œstrin or thiouracil. Diagnostic facility in sorting out the meaning of the different eye signs is increasing, both through animal experiment and clinical observation.

THERAPEUTICS

In the therapeutic field we are again concerned with advances connected with the war. Two new drugs at least have been added to our pharmacopœia, and advances in other fields of treatment, such as contact lenses and orthoptics, are also traceable to war influence.

The two drugs referred to are BAL and D.F.P. Both discoveries come from the teams of research workers on war gases. BAL (British Anti-Lewisite) (Peters, Stocken and Thompson, 1945) is a remarkable antidote to poisoning by arsenic, mercury, gold and probably other heavy metals. Its local action on the eye in preventing, and to a large extent reversing, damage by Lewisite is a completely new one and is of great interest, although its field of application is at present fortunately small. Of greater importance, however, is its systemic effect on cases of metallic intoxication, and its wider use is to be expected here. D.F.P. (difluorophosphonate) was first investigated as a possible weapon of chemical offence. Its uses here are small, but its action as a strong inhibitor of choline esterase makes it the most lasting and effective miotic known (Leopold and Comroe, 1946). It is therefore at present under trial in the treatment of glaucoma, especially the acute form. D.F.P. possesses certain disadvantages, however, and it is not proved that it is actually an advance on eserine, although its action is stronger.

Work on *contact lenses*, which received an impetus from their use in cases of mustard gas keratitis from the first world war, has advanced recently,

both because of their use to obviate spectacles in certain branches of the Services and on account of their value in the treatment of certain injuries (e.g. burns and wounds of the lids) in conjunction with plastic surgery. Many types of contact lens are now in use and the period of tolerance is increasing. Some types give a 50 per cent. wear of eight to sixteen hours a day, but knowledge of all the factors which determine tolerance is still incomplete. It is now possible, however, to classify the types of fit attainable by various methods and to relate these to types of eye and to a large extent to tolerance (Dickinson and Clifford Hall, 1946).

DIAGNOSIS

In the diagnostic field the work from the Zurich school under Professor Amstler holds first place for its originality and truly scientific approach to some of the most puzzling problems in ophthalmo-pathology (Amstler, 1948). He and his co-workers have devised a safe method of diagnostic puncture of the anterior chamber coupled with microtechniques (culturing, micro-centrifuging) for the examination of the material so obtained. In this way he has been able to demonstrate the presence of micro-organisms, to consolidate knowledge of the types of cellular reactions, to distinguish between cells derived from the ocular tissues (e.g. lens epithelial cells growing in the aqueous) and invading inflammatory cells, and to investigate the nature of the non-cellular exudates in the living human eye at stages of disease never before available for direct examination. The parallelism of his results with those of experimental workers on animals is striking, and it would seem likely that the pathology of many obscure conditions can now be tackled.

RESEARCH

In the academic field three lines of progress suggest themselves. The first, followed both in England and the United States, concerns itself with the reactions of the eye to chemical injury. Studies mainly directed to war ends have advanced our knowledge of biological reactions in a number of ways (*Bull. Johns Hopk. Hosp.*, 1948). In the first place, biochemical conceptions of the way in which certain chemical groupings affect cells have been considerably widened by studies of enzyme reactions and by investigations on the combining properties of the SH-groups in the protein molecule. In the second place, methods of healing in epithelia and in avascular tissues generally have been studied in the cornea and much light thrown on the problem of corneal scars and vascularization (Mann, Pirie and Pullinger, 1948), and thirdly, advances have been made in methods of investigation of the ocular tissues *in vitro* (survival, respiration, enzyme content, tissue culture).

The second line of progress concerns the work of Stone (1947) in the

biological field on the transplanting and regeneration of eyes in amphibia. These experiments, fantastically unexpected to those who study the human eye alone, are of vast interest to neurologists and comparative physiologists. Stone has shown that the salamander retina can regenerate entirely from the cells at the ora serrata after complete section of the optic nerve, that eyes can be transplanted and regain full function, and that eyes rotated after a certain stage retain their original spatial orientation. This work is too complicated for full notice here but is of wide significance.

A third suggestive line of work concerns the use of the eye as a medium for experiments on wider pathological problems. It has been known for some time that malignant tumour tissue can be grown and studied in the anterior chamber of animals. It is now possible to use parts of the eye to study experimental induction of tumours. For example, the lens, although clinically completely immune to malignant change, can be made to produce an epithelioma of the subcapsular epithelium by being transplanted subcutaneously together with a chemical carcinogen in inbred strains of animals with a high cancer incidence (Mann, 1947). This technique could well be extended for the study of other pathological problems.

Advances in ophthalmology therefore show a much to be desired tendency for the specialty to link itself with the techniques of biochemistry, pathology and experimental biology. Clinical ophthalmology is gaining thereby and other disciplines are afforded a relatively new experimental medium.

References

- Amsler, M. (1948): *Trans. Ophthalm. Soc.*, 68 (in the press).
Bulletin of Johns Hopkins Hospital (1948): 82, No. 2.
 Dickinson, F., and Clifford Hall (1946): "Introduction to the Prescribing and Fitting of Contact Lenses," London.
 Leopold, T. H., and Comroe, J. H. (1946): *Arch. Ophthalm.*, 36, 17.
 Mann, I. (1946): *Amer. J. Ophthalm.*, 29, 654.
 — (1947): *Brit. J. Cancer*, 1, 63.
 — (1947): *Ophthalm. Lit.*, 1, 235.
 —, Pirie, A., Tansley, K., and Wood, C. (1946): *Amer. J. Ophthalm.*, 29, Suppl. 13, 801.
 —, —, and Pullinger, B. D. (1948): *Brit. J. Ophthalm.* (in the press).
 Peters, R. A., Stocken, L. A., and Thompson, R. H. S. (1945): *Nature*, 156, 616.
 Pochin, E. E. (1944): *Clin. Sci.*, 5, 75.
 Stone, L. (1947): *Trans. Ophthalm. Soc.*, 67 (in the press).
 Wolbach, S. B., and Bessey, O. A. (1942): *Phys. Rev.*, 22, 233.

ADVANCES IN THE TREATMENT OF ORAL AND DENTAL DISEASES

By M. A. RUSHTON, M.D., F.D.S.

Professor of Dental Medicine, University of London; Assistant Dental Surgeon, Guy's Hospital.

DENTAL CARIES

The treatment of dental caries appears to have reached a stage at which only relatively small technical improvements will be possible. Most interest therefore lies in the prospects of prevention. A striking fact was the diminution in the extent of dental caries in children during the war years compared with the years preceding the war. This was observed not only in Britain but to a varying degree in all the Scandinavian countries, especially Norway and Finland, and also in Switzerland. A similar phenomenon was reported in England during the 1914-18 war. Opinion as to its interpretation is divided. On the one hand it is ascribed to the greatly improved nutrition of children in the countries of western Europe during the years preceding the war, the suggestion being that teeth of superior structure were then formed which on eruption during the war years resisted decay. The other view is that the improvement was the result of decreased consumption of sugars during the war and the disappearance of low extraction flours, the free use of these substances being known from previous surveys to be associated with a high caries rate. It appears quite probable that both explanations may be correct. The improvement in some countries is thought to have started before the war had caused any substantial alterations in diet. On the other hand, the extent of improvement in the various Scandinavian countries compared with one another is related rather to the privations endured—the more, the better the dental condition—than to the quality of their pre-war children's diets. The increase in caries in Norway which has followed the liberation could be explained on both hypotheses as regards very young children, but as regards older children the local effects of the diet are more probably to blame. The latest information on London five-year-old children shows the opposite trend (Mellanby and Mellanby, 1948), the decrease in caries observed during the war having become even more marked in the period 1945 to 1947. This was clearly not due to further restriction of refined carbohydrates and, taken in conjunction with observed improvement of enamel surfaces and the fact that the children in question were the first to benefit throughout their whole lives from access to dietary supplements promoting calcification, gives strong support to the view that better structure resulting from better infant nutrition was a very important factor.

Extensive surveys have shown that of children in any one community

those with teeth of good structure, as estimated by the physical character of the enamel surface, have less caries than those of mediocre and *a fortiori* of poor structure. There is therefore little reason to doubt that the satisfactory feeding of infants is one of the important means of reducing the incidence of dental caries. The calcification of the deciduous teeth begins *in utero* but most of the enamel formed before birth does not appear on the surface of the teeth and is covered over by enamel formed after birth. Those parts which do appear on the surface almost never form the starting point of caries. Therefore whilst good nutrition in pregnancy is from all points of view highly desirable, from the standpoint of dental caries it is probably of small benefit to the child unless the latter is breast-fed subsequently. Nutrition and health from birth to middle childhood are of the greatest importance in determining tooth structure.

Great attention has been paid in recent years to the *fluorine content of the water* in different areas, since it has been found that in areas where the fluorine content of drinking water is from 0.75 to 1 part per million the incidence of dental caries in young children is greatly reduced compared with that of similar age-groups in areas with a lower proportion of fluorine. The content mentioned is insufficient to produce unsightly "mottling" of the enamel. In several districts in the United States of America fluoride are being added to communal drinking water supplies with a view to reducing the incidence of dental caries, but information will not be available for some years as to whether or not this artificial addition has the same beneficial effects as natural waters of high fluorine content. It is only those teeth which are being formed while these natural waters are used that have been shown to enjoy some protection: fully formed teeth are not affected.

Although considerable importance is to be attached to good structure of the teeth there is clear evidence that *environmental factors* subsequent to tooth eruption play an equal or even more important part. The low incidence of caries in orphanages and similar residential institutions has long been known and it has been shown that those children of longest residence have the least caries. Since the early circumstances of many of the children were often hazardous it is not surprising that the structure of their teeth, judged by the character of the surface, is generally inferior to that of the teeth of middle-class children living at home, but they have less decay. Coumoulos and Mellanby (1947) have shown that whereas this is so, yet in any one institution those whose teeth appear of best structure have least caries. The nature of the "institutional factors" responsible for the excellent state of the teeth in orphanages and the like requires further investigation, and it cannot yet be said with any certainty whether it resides in the character of the diet or some other particulars of the regimen. The phenomenon is not, of course, peculiar to Britain, and the institutional diets vary widely. The fact that even teeth of poor structure can be prevented from decaying by a suitable habit of life is of cardinal importance, since structure can only be very slightly modified after the eruption of the tooth.

One such modification which is being widely tried is produced by the application of 2 per cent. *sodium fluoride* to the enamel surface. When this is done on four occasions within a few years of the eruption of the tooth the incidence of caries is greatly reduced—in many surveys by about 40 per cent. If recent experiments on these lines carried out in England confirm the claims made in other countries it is likely that this treatment will be applied as a routine. The anterior teeth become protected more than the posterior ones, perhaps owing to more complete accessibility, and no benefit is conferred upon areas which have already started to decay.

PARODONTAL DISEASE

The conception of parodontal disease has changed somewhat in recent years, a change which is reflected in the virtual abandonment of the old term *pyorrhœa alveolaris*. There is reason to believe that the tissue changes which result in loosening of the teeth and the formation of "pockets" between tooth and gum are not the result, as once supposed, of a bacterial invasion of the tissues but of the absorption over a considerable period of toxic products of bacterial infestation at the surface of the gum margin. From the histological standpoint the characteristic changes are present to some extent in all adults, and the appearance of clinical manifestations depends upon the speed with which they progress. The course of events seems to be as follows:—

Food debris collects in sheltered areas around the necks of the teeth and remains undisturbed owing to the non-fibrous nature of the diet and limited hygienic measures. A variety of organisms proliferates in these areas, including many thread forms which produce dense masses attached to the tooth. The calcification of such masses forms tartar which is a mechanical irritant to the gum margin and further protects the stagnation area from disturbance. The prolonged contact of tartar, food debris and organisms with the surface of the gum next to the tooth leads to failure of keratinization of the epithelium and, later, ulceration, with chronic inflammatory changes in the underlying connective tissue and the disintegration of the collagen fibres which attach the tooth to the bone. As the fibres progressively disappear they are not replaced. The epithelium grows down the root and a "pocket" is formed between the gum and the tooth. The deeper the pocket the greater is the stagnation and absorption of toxic material, so that a vicious circle is established. The resorption of bone around the tooth is a remote effect of the bacterial infestation of the gum margin and not an indication of infection of the bone.

Whilst much of this conception rests on good evidence other parts do not, and individual interpretations, such as that of Fish (1948), present a combination of knowledge and ingenious surmise.

Treatment.—In so far as a considerable amount of agreement has been reached, treatment is directed to preventing the development of stagnation areas by ensuring the proper alignment of children's teeth; to the encouragement of oral hygiene, including the use of fibrous foods; to the cleaning and friction of the interdental areas in adults by wooden points; and to the removal of tartar if and when it is found. When pockets have already formed so that stagnation cannot be prevented the situation is met by removing the free edge of the gum which forms the outer wall of the pocket,

those with teeth of good structure, as estimated by the physical character of the enamel surface, have less caries than those of mediocre and *a fortiori* of poor structure. There is therefore little reason to doubt that the satisfactory feeding of infants is one of the important means of reducing the incidence of dental caries. The calcification of the deciduous teeth begins *in utero* but most of the enamel formed before birth does not appear on the surface of the teeth and is covered over by enamel formed after birth. Those parts which do appear on the surface almost never form the starting point of caries. Therefore whilst good nutrition in pregnancy is from all points of view highly desirable, from the standpoint of dental caries it is probably of small benefit to the child unless the latter is breast-fed subsequently. Nutrition and health from birth to middle childhood are of the greatest importance in determining tooth structure.

Great attention has been paid in recent years to the *fluorine content of the water* in different areas, since it has been found that in areas where the fluorine content of drinking water is from 0.75 to 1 part per million the incidence of dental caries in young children is greatly reduced compared with that of similar age-groups in areas with a lower proportion of fluorine. The content mentioned is insufficient to produce unsightly "mottling" of the enamel. In several districts in the United States of America fluorides are being added to communal drinking water supplies with a view to reducing the incidence of dental caries, but information will not be available for some years as to whether or not this artificial addition has the same beneficial effects as natural waters of high fluorine content. It is only those teeth which are being formed while these natural waters are used that have been shown to enjoy some protection: fully formed teeth are not affected.

Although considerable importance is to be attached to good structure of the teeth there is clear evidence that *environmental factors* subsequent to tooth eruption play an equal or even more important part. The low incidence of caries in orphanages and similar residential institutions has long been known and it has been shown that those children of longest residence have the least caries. Since the early circumstances of many of the children were often hazardous it is not surprising that the structure of their teeth, judged by the character of the surface, is generally inferior to that of the teeth of middle-class children living at home, but they have less decay. Coumoulos and Mellanby (1947) have shown that whereas this is so, yet in any one institution those whose teeth appear of best structure have least caries. The nature of the "institutional factors" responsible for the excellent state of the teeth in orphanages and the like requires further investigation, and it cannot yet be said with any certainty whether it resides in the character of the diet or some other particulars of the regimen. The phenomenon is not, of course, peculiar to Britain, and the institutional diets vary widely. The fact that even teeth of poor structure can be prevented from decaying by a suitable habit of life is of cardinal importance, since structure can only be very slightly modified after the eruption of the tooth.

ADVANCES IN TROPICAL MEDICINE

A REPORT ON THE FOURTH INTERNATIONAL CONGRESS - ON TROPICAL MEDICINE AND MALARIA

By BRIAN MAEGRAITH, M.B., D.PHIL.

Professor of Tropical Medicine, Liverpool School of Tropical Medicine.

The field of tropical medicine is so vast that it is difficult, within the space of one article, to provide a balanced review of recent advances. The 4th International Congress on Tropical Medicine and Malaria, however, which was held in Washington, D.C., in May of this year, covered the field so adequately and extensively that it has been felt that no better method of summarizing the present position was available than by publishing a review of the proceedings of the congress. The subjects for discussion were divided into twelve sections and a brief account of the sessions of the more important of these sections is given below.

BACTERIAL AND SPIROCHÆTAL DISEASES

In this section there were discussions on tuberculosis, syphilis, yaws, pinta, relapsing fever, plague, enteric diseases, cholera, leptospirosis and leprosy, and electron microscopy.

Plague.—The session on plague contained an excellent paper on ecological studies of rodents in relation to plague control by Dr. D. H. S. Davis, Government Ecologist for the Union of South Africa. He produced evidence to show that sylvatic foci could be eliminated in certain circumstances in limited areas. Anti plague measures had improved considerably since the advent of new insecticides, rodenticides and baiting techniques. There was an interesting discussion on the respective merits of living and dead plague vaccines, in which opinions differed sharply. A particularly interesting point was raised by Professor Karl Meyer of San Francisco, who suggested that the superior protective power of certain living avirulent strains of *Pasteurella pestis* resulted from the invasiveness and survival of the organisms in the tissues "to which they impart a more active and probably more lasting effect on the important cellular immunity mechanism than does the injection of dead organisms or antigens." The general impression was that a fully effective vaccine for endemic plague had not yet been produced.

Cholera.—The composition and efficacy of cholera vaccine was discussed by Dr. Pandit of Madras, India. Statistical evaluation of the vaccine in the prevention and control of cholera epidemics had been made during the epidemic in Southern India of 1942-43. In a population of over three millions in which there were 35,000 cases of cholera, the incidence of the disease in the uninoculated was fourteen times greater than in the inoculated group. The economic, nutritional and sanitary status of the individual

and this gives the patient, as it were, a fresh start. Recurrence, however, can usually be prevented only if the patient will cooperate assiduously. Of the population as a whole the proportion willing to take the necessary trouble, although increasing, is limited, and this is one reason why the alternative of extracting the teeth is still so often applied at a stage when this last resort would not otherwise be indicated. Other reasons are that in many cases medical practitioners have been accustomed to advise the removal of teeth when the gums showed signs of chronic inflammation, being unaware that the matter could be dealt with in another manner; and dentists have sometimes not been averse from taking this easy course when it might have been avoided. There is little doubt that at the present time far too many teeth are still being extracted, and whilst much blame can be laid on patients who neglect to obtain treatment until it is too late or who are unwilling to cooperate in treatment, much responsibility also rests upon those medical and dental practitioners who have seen in parodontal disease a focus of infection for which there was only one drastic remedy.

Although the local factors mentioned, together with others not cited here, appear sufficient to account for the disease in many individuals, the rate at which it advances is influenced by constitutional factors and intercurrent diseases. Some causes of acceleration, such as diabetes and scurvy, senility, and sometimes pregnancy, are well recognized, but others remain obscure and the subject of speculation. A comprehensive review of knowledge of the effects of nutritional factors has recently been presented by King (1948). In a rapid form sometimes seen in young persons, usually girls, an underlying constitutional cause is often sought in vain, although sometimes coexistent disorders are found. In such persons conservative local treatment may be ineffective.

The introduction of local *penicillin therapy* (MacGregor and Long, 1945) for acute ulcerative (Vincent's) gingivitis has provided a successful method for the rapid alleviation of symptoms, and has become so well known that little need be said about it. Whether pastilles, lozenges or chewing gum be used does not seem of great importance, and additional parenteral administration in severe cases is a reasonable measure. What is important is that treatment should not be confined to the alleviation of symptoms by these means but should be followed by adequate dental treatment to prevent their recurrence. This may entail the removal of half-erupted teeth, deep pockets, and the like. The discomforts which some patients may suffer as a result of using penicillin lozenges continuously for more than two or three days—e.g. penicillin sore-tongue—are now well recognized.

References

- Coumoulos, H., and Mellanby, M. (1947): *Brit. med. J.*, i, 751.
Fish, E. W. (1948): "The Surgical Pathology of the Mouth," London.
King, J. D. (1948): *Nutr. Abstr. Rev.*, 17, 569.
Macgregor, A. B., and Long, D. A. (1945): *Brit. dent. J.*, 78, 33.
Mellanby, M., and Mellanby, H. (1948): *Brit. med. J.*, ii, 409.

variola and yellow fever vaccine. The two viruses were mixed at the time of vaccination in a solution of gum arabic and the mixture was applied to the skin as in ordinary vaccination. More than twenty million persons had been vaccinated in this way up to January 1948, with very satisfactory results. A high percentage of vaccinated individuals showed adequate protective antibodies in the serum.

Phlebotomus fever.—Dr. A. B. Sabin described attempts to identify strains of phlebotomus fever viruses. These viruses were studied by inoculation of human volunteers with serum from patients with self-limited febrile illnesses of short duration. Only phlebotomus fever viruses were recovered from the Mediterranean area and only dengue viruses from the Pacific area. Two strains of phlebotomus fever virus, one originating from the Middle East and the other from Sicily, proved to be immunologically identical. A third, originating in Naples, was totally distinct from these two. The phlebotomus viruses could not be cultivated in embryonated eggs, nor in any laboratory animal. Immunity to homologous virus was found to be of long duration. Studies on ten strains of dengue virus from Hawaii, New Guinea, India and Japan revealed the existence of three distinct related immunological types. The Hawaii virus occurred also in New Guinea, India and Japan. There was a group relationship between the different immunological types of dengue virus, and recovery from infection with one type conferred complete resistance to other types for a period of one to two months, and a partial resistance for eight months or longer. A mouse adapted virus has made serological tests for dengue possible.

Poliomyelitis.—There was a first-class discussion on tropical poliomyelitis. Dr. J. H. S. Gear reported that in a recent epidemic in South Africa the virus was isolated from faeces of children in native villages where there was no clinical evidence of the disease. An immunity survey had been carried out using the Lansing strain mouse protection test. In all age-groups the African proved to have a higher percentage of immunity than Europeans. The higher rate of paralytic poliomyelitis in Europeans was noted by several speakers during the discussion.

Neotropic viruses.—Dr. K. C. Smithburn gave an interesting account of isolation of neurotropic viruses in East Africa. During the past ten years eight such viruses, each distinct from the other and from all other previously recognized viruses, had been isolated by the group of Rockefeller Foundation workers at Entebbe, Uganda. Five viruses had been carefully studied, and each induced the formation of neutralizing antibodies and gave clear-cut protection tests. Immunity to each has been observed in humans and in wild animals, notably primates. The clinical manifestations of infections by these viruses in humans were not well known.

Rabies.—The problem of eradication of rabies in wild animals was dealt with by Dr. H. M. Johnson of New York, and in the subsequent discussions there was considerable comment on the need for standardization and improvement of rabies vaccine.

appeared to affect the degree of protection obtained after inoculation. The Haffkine Institute had prepared a vaccine by growing the vibrio in casein hydrolysate medium. Large-scale field trials with this new vaccine were contemplated.

Leprosy.—The discussion on the chemotherapy of leprosy revealed a certain difference of opinion with regard to the use of chaulmoogra oil and other hydnocarpus remedies. Dr. Frederick Johansen, Director of the National Leprosarium, Carville, Louisiana, stated that in his experience only chaulmoogra oil and the sulphones had proved satisfactory. Streptomycin was of doubtful value for systemic treatment but of some value employed locally. He had entirely abandoned chaulmoogra oil treatment in favour of sulphones. Sulphones had replaced chaulmoogra oil in Carville, chiefly because of their superior therapeutic action demonstrated in early as well as in advanced lepromatous leprosy. The sulphone drugs were not specific remedies, and rapid and spectacular cures were not to be expected from their use; but there was almost universal improvement and the disease seldom, if ever, became worse during treatment. Objective clinical improvement did not appear for three to six months after treatment, but subsequent improvement was progressive, with few, if any, relapses. Clinical improvement was followed by a reduction in bacilli in the leprous lesions, and simple atrophy of the morbid anatomical changes in the skin and mucous membranes. The drugs were of low toxicity. Dr. Robert G. Cochrane, Vellore College, India, on the other hand, stressed the importance of chaulmoogra treatment and laid emphasis on treatment of the skin in the therapy of leprosy. He pointed out that dosage and administration of sulphone drugs should follow the principles of chemotherapy in general, and suggested that the chemotherapy of leprosy should be considered from four points of view:—(1) practicability of administration; (2) rapidity of action; (3) accumulation in the tissues, especially the skin; and (4) availability to the large masses who could never be admitted to a leprosy institution, but who attended hospitals and out-patient's clinics. The value of treatment with hydnocarpus products had become more obvious following recent developments in the technique of their administration. In mass treatment in the field there was still a definite place for chaulmoogra oil.

VIRUS AND RICKETTSIAL DISEASES

Scrub typhus.—During the discussion on rickettsial disease an interim report was read on the treatment of typhus with chloromycetin, which was being tested in clinical trials at Kuala Lumpur in Malaya. In a small series of cases of scrub typhus Dr. J. E. Smadel and Dr. R. Lewthwaite reported most promising results. A very optimistic view was taken of the possible use of this antibiotic in other rickettsial infections.

Yellow fever.—Discussion on the epidemiology of yellow fever and its control included a paper by General M. Peltier, Director General of Public Health in French West Africa, who described the extensive uses of combined

tered once a week would provide adequate protection. Dr. L. T. Coggeshall, University of Chicago, discussed the cure of recurrent vivax malaria and the status of immunity thereafter. The patients examined were treated with 2 gm. of quinine in combination with 60 mgm. of pentaquine daily for two weeks. Patients who could be considered to have acquired a partial degree of immunity required a smaller daily dosage of pentaquine (30 mgm.). Eighty patients, some of whom had experienced as many as 30 relapses, had been treated on this regime and followed for a sufficient period of time to indicate that their malaria had been eradicated. Only one failure had occurred. Dr. Coggeshall found that the degree of immunity after reinfection with homologous strain sporozoites bore a positive relation to the number of relapses prior to reinfection. The duration of immunity following cure was variable but in general relatively mild.

The general discussion on chemotherapy struck an optimistic note. Professor Rodhaim, however, stressed the importance of long-term observation with regard both to the ultimate assessment of the value of a drug and its possible toxicity.

The fourth session of the section on malaria dealt with immunity and contained an interesting paper by Professor Taliaferro, University of Chicago, who discussed the characteristics of acquired immunity. Dr. Taliaferro saw little hope that there would be any development of potent antisera or dead vaccines for the widespread control of malaria, chiefly because of the large numbers of antigenic variants in each species and the large amounts of antigen required to produce active immunization, together with the short duration of immunity so produced.

HELMINTHIC DISEASE

Recent developments in the chemotherapy of helminthic diseases were discussed by Dr. H. W. Brown, School of Public Health, Columbia University, New York. The modern search for new anthelmintics followed in general "a pattern of *in vitro* tests on related helminths and *in vivo* trials on infected animals, accompanied by pharmacological and toxicological studies," and followed by experimental trials on infected humans. Arsenamide and hetrazan for filariasis, and lubisan and phenothiazine for enterobiasis were new chemotherapeutic agents of some activity, resulting from such studies. A number of agents of established value in protozoal infections had also been found of use in worm infections. Neostibosan, for instance, was active in Bancroftian filariasis, atebirin in tæniasis and emetine hydrochloride in trichuriasis. Similarly, anthelmintics effective against one group of helminth parasites had been found active against other groups. Thus, anthiomaline, which was known to be active against schistosomiasis, was also useful in filariasis. There was a good discussion on schistosomiasis and its control, during which Dr. Abdel Azim, Ministry of Health, Cairo, pointed out the great need for a potent, cheap, and water-soluble mollusci-

MALARIA

The discovery of the pre-erythrocytic cycle of *Plasmodium cynomolgi* was described by Professor H. E. Shortt of the London School of Hygiene and Tropical Medicine. This was the outstanding original communication to the congress and was one of great importance to malarial parasitologists. Professor Shortt was awarded the Laveran medal for his work in connexion with this discovery.

Chemotherapy.—The drugs discussed were chloroquine, pentaquine, isopentaquine and paludrine. Dr. D. P. Earle, New York, stated that the most active of the 4-amino-quinoline compounds tested by the Americans during the war was chloroquine. This drug was more active than atebirin on the basis of either oral dosage or effective plasma drug concentration. It was less toxic than atebirin or quinine in relation to effective therapeutic dosage. It was active against trophozoites of several strains of *P. vivax* and *P. falciparum*, but unfortunately had no demonstrable effect on *P. vivax* tissue parasites and thus no effect on relapsing malaria. It was a highly effective suppressive agent, small weekly doses preventing the development of clinical attacks of vivax or falciparum malaria. Dr. A. S. Alving, University of Chicago, described the use of pentaquine and isopentaquine. Preliminary investigations indicated that isopentaquine had the greater range between the therapeutic and the maximum tolerated dosages. On equal dose basis it was more effective as a curative agent than pentaquine. "The concurrent administration of 10 mgm. pentaquine base and 330 mgm. quinine sulphate every four hours throughout every twenty-four hours for fourteen days had reduced the relapse rate in infections of S.W. Pacific (Chesson) vivax malaria from 98 per cent. after suppressive drugs to about 25 per cent. in experimental volunteers. After a second therapeutic course relapses were reduced to 2 per cent." There were some toxic manifestations on 60 mgm. base daily, roughly equivalent to those experienced after the administration of 30 to 45 mgm. pamaquine base. Acute hæmolytic anæmia occurred in approximately one in 150 cases. In less heavily infected or partially immune white subjects the daily dose of pentaquine could be halved and the toxicity was then practically *nil*. The use of paludrine in the treatment and suppression of malaria was described by Professor B. G. Maegraith, Liverpool School of Tropical Medicine. Paludrine represented a group of compounds which had not previously been known to be antimalarial in action. In adequate doses it acted as a causal prophylactic in *P. falciparum* infections and as a suppressive in *P. vivax* infections. It was very active therapeutically in all forms of human malaria. Administered by itself it had no effect on the relapse rate of *P. vivax* malaria. This relapse rate could, however, be considerably reduced by the concurrent administration of 100 mgm. paludrine and 10 mgm. pamaquine, three times daily for ten days. The best prophylactic and suppressive dose was 100 mgm. daily, but for labour groups a single dose of ---

tion of substances which did not produce resistant strains, and in the treatment of early cases with substances which could limit the attack effectively after a few doses, and also protect populations by a long-lasting preventive action.

Chagas' disease.—The problems of Chagas' disease and its control were discussed by Dr. Diaz, Brazil. Vectors of this disease are widely spread in the Americas, and infection is transmitted by faecal contamination. *Schizotrypanum cruzi* has frequently a characteristic action on the heart; about 50 per cent. of cases in some areas show evidence of cardiac damage, which may be fatal. Disturbance of cardiac rhythm, right bundle branch block, ventricular premature beats, with auricular-ventricular blocks, are particularly important. In cardiac patients death occurs commonly from heart failure, and sudden death is frequent. Infection can last for years. Prophylaxis should aim principally at the suppression of insect vectors, but educational measures were also of great importance.

NUTRITIONAL DISEASES IN THE TROPICS

The background problems of nutrition in the tropics and the nutritional deficiencies and problems of special areas in the tropics were discussed. The problems of India, China, South East Asia, the American tropics and South Africa were stressed. One of the most stimulating contributions was that of Drs. Theodore and Joseph Gillman, University of Witwatersrand, South Africa. They reported that chronic malnutrition is widespread amongst the poverty-stricken South African negroes, among whom there is an almost epidemic frequency of pellagra and associated nutritional diseases. Severe fatty livers in infants and iron-containing and cirrhotic livers in adults were revealed by liver biopsies. Nutritional changes of this sort should be regarded not as specific vitamin deficiencies but as the effects of the peculiar metabolism imposed on the body by the continued consumption of a grossly inadequate diet. The authors regarded diet as a metabolic stimulator, the type of metabolism imposed by the diet being determined largely by its content. The biological effects of a foodstuff depended upon its concentration in the diet and upon the nature of the other constituents in the diet. Since biological effects of food could not be estimated at the moment on the basis of chemical constitution they doubted whether we were at present in a position to "impose on the population nutritional supplements such as vitamins on the basis of chemical analysis of the diet. Such an approach to supplementary feeding may result in much damage." They stressed the need for further experimental work on the problem of supplementary natural diet before adequate substitutes could be suggested for good food.

TROPICAL DERMATOLOGY AND MYCOLOGY

The general problems of mycology, including those of histoplasmosis and

cide which was not toxic to higher animals or crops. Widespread application in Egypt of antimony treatment over thirty years had not succeeded in reducing the incidence and development of bilharziasis. A drug which acted quickly and which could be given in one injection or in a few oral doses would be most valuable. Radical changes in social conditions were necessary before health propaganda and the prevention of soil and water pollution could hope to be effective. Among other subjects discussed were the metabolism of *Schistosoma mansoni* and the etiology of hookworm anæmia, which, according to Dr. W. O. Cruz, Brazil, was basically a deficiency disease.

PROTOZOAN DISEASE

There were two sessions of this section during which amoebiasis and the blood and tissue flagellates were discussed.

Amoebiasis.—Dr. S. L. Chang, Harvard University, described the experimental physiology of amoebiasis and referred to the fact that amœbæ have been propagated for weeks in anaerobic bacteria-free culture with fresh liver. The establishment of amoebic infection in human beings or animals was connected with the anaerobic requirements of the organism, which might possibly explain the localization of amoebic infection in the large bowel. Profound anaerobiosis in the intestines seemed to pave the way for amoebic invasion of the tissue. Mr. W. R. Jones, Imperial Chemical Industries, England, discussed experimental chemotherapy of amoebiasis and described his interesting technique for the production of extensive amoebic ulceration of the large intestine in rats. In animals infected in this way, chemotherapeutic studies of possible anti-amœbic compounds can be quickly and easily carried out.

Dr. C. A. Hoare, Wellcome Laboratories, discussing the relationships of the hæmoflagellates, pointed out the necessity for revision of the zoological classifications of the leishmanias and trypanosomes, and proposed a revised classification for mammalian trypanosomes.

Kala-azar.—Dr. P. C. Sen Gupta, Calcutta School of Tropical Medicine, India, gave an account of researches on kala-azar in India over the last ten years. In his view the combination of mass treatment for leishmaniasis and the use of DDT for sand-fly control offered the best chances of control of kala-azar.

Trypanosomiasis.—Dr. L. Van Hoof, Antwerp, Belgium, pointed out that the chemotherapeutic battle against trypanosomiasis had not completely succeeded in eradicating the disease, since there was a residual febrile incidence, which was apparently irreducible. This was probably due to resistance on the part of the parasite to the chemical substances employed. Such resistance might finally render the principal current trypanosomicidal substances useless. The entomological struggle against human trypanosomiasis was equally incomplete. The hope of the future lay in the utiliza-

CURRENT THERAPEUTICS

X.—THE CLINICAL USE OF GAMMA GLOBULIN

By CHARLES A. JANEWAY, M.D.

*Thomas Morgan Rotch Professor of Pediatrics, Harvard Medical School;
Physician-in-Chief, the Infant and Children's Hospitals, Boston, Mass., U.S.A.*

Normal serum gamma globulin, usually known as "gamma globulin" and officially called *immune serum globulin* in the United States, is a concentrated solution of the antibody fraction of pooled normal human plasma which has come into general use there for passive immunization against certain infectious diseases, particularly measles. It is one of the products of plasma fractionation, a process developed during the war by Professor Edwin J. Cohn and his colleagues (1946) for the separation of the various functionally important plasma proteins into a series of fractions, in each of which an important physiological activity of the plasma is concentrated and from which products may be prepared which preserve this activity in stable and convenient form for therapeutic use. These products include Fraction I or "antihæmophilic globulin", fibrinogen, fibrin film, fibrin foam, thrombin, gamma globulin, blood-grouping (anti-A, anti-B, and anti-Rh) globulins, and serum albumin. Over 2 million of the 13½ million voluntary blood donations to the Red Cross by the people of the United States during the war were subjected to fractionation. Gamma globulin surplus to the needs of the Army and Navy was returned to the American Red Cross and has been distributed by them since 1944 through public health agencies to the physicians of the United States for the control of measles, and directly to investigators for study of its value in other conditions. It is also prepared by one commercial laboratory,* which has entered the field of plasma fractionation. This review is an attempt to summarize the present state of our knowledge concerning this new biological agent.

As now prepared from Fractions II and III of human plasma by methods developed by Oncley and his colleagues (1948), gamma globulin is packaged in 2 c.cm. vials, containing a 16.5 per cent. solution of protein (more than 90 per cent. of which is gamma globulin) in a glycine diluent, since this gives greater stability than sodium chloride. Such a solution is rather viscous, but can be readily injected through standard intramuscular needles, and usually looks water-clear, although it may be slightly opalescent. The concentration of gamma globulin in this solution is 25 times that in pooled normal human plasma, and most of the antibodies present in the plasma pool should be concentrated 20-25 times in the globulin solution. Careful laboratory tests made on each globulin preparation as reported by Enders (1944) show that this is usually the case for typhoid H agglutinins, influenza A virus neutralizing antibodies, and diphtheria antitoxin. Unfortunately,

*Cutter Laboratories—Berkeley, California.

the status of immunobiological tests in mycoses, were discussed. An account was given by Dr. John V. Ambler, Denver, Colorado, of atebtrin dermatitis, in which he distinguished three main clinical types:—(1) the lichenoid eruption; (2) the symmetrical eczematoid, which was the most common; and (3) the exfoliative. The cutaneous manifestations of atebtrin intolerance were complex and bizarre. Symmetry was prominent in all stages and types. The distribution was characteristic: the dorsal aspect of the hands, the legs and the feet being the sites most frequently involved. Response to the withdrawal of the drug was slow. Several months may be necessary before improvement is noted. The eczematoid lesions responded most rapidly. Dr. A. L. Carrion, School of Tropical Medicine, Puerto Rico, discussed modern trends in the treatment of *Granuloma venereum*. Methods of treatment employed in dealing with this difficult disease included intensive antimony treatment and streptomycin.

PUBLIC HEALTH

Dr. J. D. Aronson, United States Public Health Service, discussed B.C.G. vaccination in the control of tuberculosis. He described a study carried out amongst Indians living on four widely separated Indian Agencies and in communities in South-Eastern Alaska. The group vaccinated with B.C.G. totalled 16,406 person-years, the control group, 15,207 person-years. The death rate from tuberculosis amongst the first group was 0.4 per 1000 person-years, and amongst the control group 3.0 per 1000 person-years. At the end of the nine to eleven years' period of observation, the tuberculin reaction was positive in 93 per cent. and 42 per cent. of the vaccinated and controls, respectively. This work indicated that the use of B.C.G. was a safe and practicable procedure which significantly reduced the mortality of tuberculosis in a highly infected population.

MEDICAL AND VETERINARY ENTOMOLOGY

The sessions in this section contained communications and discussions which were often closely linked with those of other sections of the Congress. The control of mosquitoes and other flies, including *Phlebotomus* and *Glossina*, especially by DDT, was discussed in considerable detail. Ticks, mites, lice and fleas were discussed separately in the third session, which contained a communication by Dr. C. B. Philip and Dr. G. M. Kohls, U.S. Public Health Service, on the relations of mites to the spread of scrub typhus. Dr. R. C. Bushland, U.S. Department of Agriculture, discussed the question of insecticides in the control of lice attacking man and animals, and stated that recent experiments on oral administration of insecticides which rendered the blood of the host toxic to lice showed considerable promise of chemotherapeutic control. The fourth session dealt with triatoma, insecticides, toxicology, and the equipment necessary for applying insecticides.

possible to study reports from a large number of cases and to establish figures for optimal dosage.

Dosage.—Provided gamma globulin is administered in the first eight days after exposure, the dose of globulin will make more difference than the day on which it is given. Ordinarily it is given between the third and sixth days, since the rash in the primary case does not appear until after several days of prodromal illness and is usually the signal which warns the family and physician. In these circumstances a dose of 0.1 c.cm. or more per pound of body weight will usually prevent the disease, although an occasional mild case may ensue. If modification rather than prevention is desired, a dose of 0.02 c.cm. per pound will be followed by mild measles in 60 to 70 per cent. of those exposed, by typical measles in a few and by no measles in 25 to 30 per cent. There may be some reduction in dosage necessary for modification in the waning period of an epidemic, but these figures have been substantiated during a four-year period all over the United States, and in one of those years in Great Britain and Australia. The reliability of gamma globulin in the prevention of measles is such that it has radically altered the practice in children's and fever hospitals when a case of measles is accidentally admitted to, or develops in, the ward. Formerly, the ward was closed to all but those known to be immune to measles for two weeks after the case had appeared. Now, the patient with measles is isolated as before, but the remainder of the susceptible children are given gamma globulin (0.1 c.cm. per pound) and new patients are admitted to the ward without any delay. If any of the exposed children develop mild measles, the susceptibles are all given gamma globulin again, since the effect of a single dose lasts only for from two to four weeks, but this is rarely necessary.

Septic complications are markedly reduced in measles modified by gamma globulin. It is not known whether or not the frequency of encephalitis is reduced, but it seems probable that it is. Whether modified measles confers permanent immunity or not requires further study. At present, the evidence suggests that it does to most individuals, but that in a few, second attacks of measles may occur within a year or two of what seemed to be a mild attack.

Gamma globulin, in very large doses, given soon after the onset of the prodromal stage of measles, may have some ameliorating effect on the course of the disease, but has been little used. The advantages of gamma globulin over convalescent serum, placental extracts, or even normal plasma or blood, are its availability, safety, uniform potency and stability, and the fact that such small doses are necessary (e.g. 1 c.cm. is a modifying dose for a 50 pound child).

GERMAN MEASLES

Interest in rubella, as a disease rather than a mere nuisance, has mounted steadily since the demonstration in Australia and its confirmation elsewhere

there is no *in vitro* test for the concentration of the measles protective antibody, but these laboratory tests have been carried out routinely as the most convenient indices of the general potency of the product. Uniformity is guaranteed by the fact that adults are used as donors, that the starting pools of plasma are large, and that material from 5000 to 10,000 bloods is usually combined in each lot of gamma globulin.

SAFETY AND REACTIONS

The safety of gamma globulin, as used for measles prophylaxis, has been well established, and well over a million doses have been given in the past four years. It is administered intramuscularly, and should not be used intravenously, since intravenous injections, particularly in sick children, may give rise to serious vasomotor changes and hyperpyrexia. Doses as large as 50 to 100 c.cm. have been given in multiple sites to one individual without untoward effects, other than local discomfort. A few instances of local stiffness and soreness, due primarily to the size of the dose, and an occasional episode of low-grade fever or slight malaise comprised the reactions observed in over 1000 cases, except for a single case of angio-neurotic oedema the day after injection. The over-all reaction rate was recorded as between 1 and 2 per cent. in this series, far lower than with the placental extracts* previously used for measles prophylaxis. A further element of safety lies in the apparent freedom of gamma globulin from contamination with the virus of homologous serum hepatitis (Janeway, 1945). Although certain viruses can survive the manipulations of the fractionation process and the starting pools of plasma are so large that contamination of nearly every lot seems almost inevitable, homologous serum hepatitis has only been observed after the injection of Fraction I and not after gamma globulin or serum albumin.

The following details of clinical experience with gamma globulin in the control of infectious disease are based on the work of a large number of physicians, to whom it is impossible to give due credit in this limited space. Dr. Joseph Stokes, jun. (1947), Professor of Pediatrics at the University of Pennsylvania, has done more than anyone to establish the value of this blood derivative in the prevention of disease.

MEASLES

In the United States, gamma globulin has become the standard agent for the modification or suppression of measles in exposed children. A number of studies have clearly proven its value for this purpose. By having such a large amount of material available, of fairly uniform potency, it has been

*Placental extract, formerly known as *immune globulin, human*, is now known as *immune serum globulin* if it is prepared from placental blood and conforms to the same specifications as gamma globulin derived from normal plasma.

MUMPS

The failure of normal serum gamma globulin to have any preventive power in mumps has been proved, but is puzzling in view of the apparent immunity of infants during the first six months of life. Complement fixing antibody to mumps virus, which can be measured, is present at a very low titre in the blood of most adults, whereas it reaches high titres for a month or two during convalescence. Hence the failure of normal serum gamma globulin may be due to a lack of sufficient antibody.

Gamma globulin prepared from a pool of *convalescent* mumps plasma, and having a much higher complement-fixing titre than *normal* serum gamma globulin, was shown to reduce markedly the incidence of orchitis when given in 20 c.cm. doses to alternate soldiers admitted on the first day of parotitis (Gellis *et al.*, 1945).

POLIOMYELITIS

Gamma globulin has the power to protect animals against the Lansing strain (adaptable to mice and cotton rats) of poliomyelitis virus, even when given after the virus. Its experimental trial in the prevention of human poliomyelitis, with the low attack rate of paralysis and the probable immunological differences between strains of the virus, constitutes such a formidable undertaking that it has never been attempted. A carefully controlled study of its value in the treatment of the disease, when given in massive doses, to alternate children admitted in the pre-paralytic stage, confirmed all previous controlled studies of the value of convalescent serum: that is, it had no effect whatsoever on the ultimate outcome (Bahlke and Perkins, 1945).

SCARLET FEVER

A low titre of antitoxin to the erythrogenic toxin of the β -hæmolytic streptococcus is present in normal plasma and the concentration process results in material with a considerably higher antitoxin titre than scarlet fever convalescent serum. Although large doses of gamma globulin may have some therapeutic effect in scarlet fever, the brilliant response of hæmolytic streptococcus infections to penicillin has diminished interest in serum therapy.

PERTUSSIS

In pertussis, antibody levels in normal adults are very low, but hyperimmunization of adults with pertussis vaccine gives high antibody levels. Such hyperimmune human serum is extensively used for the prevention and treatment of the disease in infants (Felton, 1945). "Hypertussis" is a gamma globulin produced by Cutter Laboratories from hyperimmune serum, thus reducing the required dose from 80-100 c.cm. to 8-10 c.cm. (Lapin, 1945).

that when the disease occurs in early pregnancy it may produce serious developmental defects in the foetus. Methods for protection of the mother and foetus from the disease during the first four months of pregnancy are therefore urgently needed. Several studies of the value of gamma globulin for this purpose are now under way, but it is too early to draw any conclusions from them.

HEPATITIS

Infective hepatitis.—Stokes and his colleagues first tried gamma globulin against this disease in the midst of a very severe outbreak, probably water-borne, in a summer camp for children. Not only was the disease prevented in most of those injected during the incubation period, but when it did develop it was modified, since the majority of those injected who did develop symptoms had what appeared to be hepatitis without clinical jaundice. These workers then made a far larger trial in Italy, when hepatitis was raging among units of the American Army, and obtained a marked reduction in the incidence of jaundice in inoculated troops as compared with uninoculated controls. As in the case of measles, although the prophylactic effect of gamma globulin, given to exposed individuals during the incubation period, was striking, it had little effect as a therapeutic measure once the disease had developed. Stokes's results have been confirmed by Paul and Havens, who studied a large outbreak in an orphanage.

Gamma globulin is not recommended for routine use in the *prophylaxis* of infective hepatitis, but can be very useful in large institutional or military outbreaks, or in special cases, such as in pregnant women who have been exposed to the disease and in whom it might present special hazards. The preventive dose appears to be the same as in measles (0.1 c.cm. per pound body weight).

Homologous serum hepatitis.—Impressed by the lack of cases of homologous serum jaundice following the injection of gamma globulin for measles prophylaxis, Stokes and his group have expended a great deal of effort in determining whether or not it might prevent this other form of hepatitis as well as ordinary infective hepatitis. Studies have been carried out in volunteers and were also made among wounded military personnel returning to large general hospitals in the U.S.A. The results so far have been somewhat confusing and variable.

CHICKENPOX

Unfortunately, since it would solve a major problem of cross-infection in children's hospitals, gamma globulin does not have an appreciable prophylactic effect in chickenpox. This is perhaps not surprising, since gamma globulin is derived from normal plasma, and infants, who receive a large passive transfer of antibody from their mothers *in utero* by way of the placenta, do not have an immunity to chickenpox, as they do to measles.

REVISION CORNER

THE TREATMENT OF CORYZA

THE nasal obstruction, rhinorrhœa, and sneezing, the symptoms of the common cold or acute infective catarrh of the upper respiratory tract, are known as coryza. There are other conditions which simulate the common cold, the most common of which are allergic vasomotor rhinorrhœa and influenza. Allergic vasomotor rhinorrhœa results in hay-fever-like attacks coming on early in the morning and remaining for a variable time, but it may suddenly disappear and the nose resume its normal condition.

When the common cold is severe and accompanied by fever, illness and prostration, also when these symptoms become epidemic and of the explosive type and the nasal symptoms are late in onset, it is usually called influenza. Influenza is now considered to be due to virus A or B infection, to which is added a secondary infection by such organisms as the streptococcus and the pneumococcus. These latter organisms are responsible for complications such as otitis media, laryngitis, and pneumonia. The diphasic temperature chart and relapses are said to be characteristic of influenza. The common cold is often preceded by acute tonsillitis or pharyngitis.

The treatment of the common cold or upper respiratory catarrh can be conveniently divided into (1) the immediate treatment, (2) the prevention of infection, and (3) the increase of the resistance and of the immunity of the patient.

GENERAL TREATMENT

The immediate treatment is one of masterly inactivity. The patient is put to bed and isolated in his own room, particularly if there is pyrexia. He should be given as much fluid as he can drink and made as comfortable as possible. The compound tablet of codeine or Dover's powder at night adds to his comfort. It is recognized that there is at present no specific treatment which arrests or suddenly cuts short an acute catarrhal attack. The fact that there are numerous and various remedies in vogue and not one single and generally adopted treatment indicates that a successful remedy has yet to be discovered. Aspirin and whisky, sodium salicylate, quinine, urotropine and cinnamon, have all had their popularity. These are now replaced by the sulphonamides and penicillin. Sulphadiazine or sulphamerazine are now the most popular. If penicillin or a sulphonamide is prescribed it is useful to have the secretion or sputum examined for the organism. For example, if the pneumococcus is present, sulphapyridine is indicated. A pneumococcal infection of the nose is quite frequent and sometimes precedes pneumonia. This infection appears to have a characteristic clinical picture. The catarrh or cold is severe, the pus is thick greenish yellow, and it is the type of cold which spreads to every member of the household. The onset is sudden, sometimes with a rigor, the temperature is high, and the infection subsides suddenly and almost by crisis. Pneumococci can be cultivated from the nasal secretion. Suppuration of the nasal sinuses, particularly of the antrum, occurs in these cases.

LOCAL TREATMENT

The local treatment of the nose by lotions and sprays is of doubtful value and may cause discomfort. Lotions and sprays are unpopular because it is claimed they wash away the protecting nasal mucus and interfere with the ciliary action of the mucosa. If used forcibly there is the possibility of driving the infection into the Eustachian tube or a nasal sinus. However, a steam inhalation of menthol and benzoin is useful. Penicillin lozenges and sprays often cause irritation even for a week or two after the application has been stopped. In my experience the local application of sulphathiazole or penicillin in the acute stage has not been very successful. Systemic penicillin injected in full doses is beneficial. When the nasal obstructions and symptoms are

INFANTILE DIARRHŒA

Trial of gamma globulin in several outbreaks of epidemic infantile diarrhœa has given no evidence of its value, which is not surprising in view of the universal susceptibility of infants to this infection.

SUMMARY

Normal human serum gamma globulin provides the physician with a stable solution of normal human antibodies ready for intramuscular injection, so concentrated that each cubic centimetre is equivalent to 25 c.cm. of pooled normal plasma, but free of the inconvenience and danger of administration in that form. It contains only those antibodies present in the plasma from which it was prepared and will only act against those diseases for which antibodies are present in adequate amounts. Its value in the prevention and modification of measles and infective hepatitis in exposed individuals has been clearly demonstrated, but it has little therapeutic value once the disease has begun. It will not prevent mumps, chickenpox, or epidemic infantile diarrhœa, but, in the case of mumps, gamma globulin prepared from convalescent plasma has been shown to lower the incidence of complications when administered early in the disease. Gamma globulin, given as early as possible, does not alter the course of poliomyelitis. Gamma globulin prepared from the serum of adults who have been hyperimmunized with *H. pertussis* vaccine is of value in passive immunization against whooping-cough.

References

- Bahlke, A. M., and Perkins, J. E. (1945): *J. Amer. med. Ass.*, **129**, 1146.
Cohn, E. J., et al. (1946): *J. Amer. chem. Soc.*, **68**, 459.
Enders, J. F. (1944): *J. clin. Invest.*, **23**, 510.
Felton, J. (1945): *J. Amer. med. Ass.*, **128**, 26.
Gellis, S. S., McGuinness, A. C., and Peters, M. A. (1945): *Amer. J. med. Sci.*, **210**, 661.
Janeway, C. A. (1945): *Bull. N.Y. Acad. Med.*, **21**, 202.
Lapin, J. H. (1945): *J. Pediat.*, **26**, 555.
Onclay, J. L., et al. (1948): (In preparation.)
Stokes, J., jun. (1947): *Ann. intern. Med.*, **26**, 353.

fections, such as trachoma. This, however, is not borne out by the experience of ordinary clinical practice, when the use of these drugs is found to be very useful in the treatment of acute and chronic conjunctivitis due to the common pyogenic organisms. Sodium sulphacetamide drops, 30 per cent., can be used three times daily, and the 15 per cent. ointment is useful in cases of chronic conjunctivitis when it can be inserted in the eyes at night over long periods. Sulphathiazole ointment and drops may also be useful. These preparations may cause complaints of discomfort from patients when they are instilled in the eyes, but this irritation is not usually a marked feature. The sulphonamide group of drugs taken by mouth or applied locally is useful in the treatment of trachoma. Full dosage by mouth and locally in the early stages, with expression of the follicles, gives satisfactory results and, although a cure cannot be guaranteed, this class of drug offers a better prognosis than any treatment previously employed for this disease.

Gonococcal ophthalmia has ceased to be a serious problem as a result of the use of penicillin and of the sulphonamide group. Penicillin can be used prophylactically in place of silver nitrate at the time of birth, and is also useful in the established condition, when it can be given locally or systemically. Sulphamezathine, given in an initial dose of 0.25 gm. and subsequently 0.125 gm. in the milk feeds, every four hours until forty-eight hours after clinical cure, is most useful in the management of gonococcal ophthalmia. In association with saline irrigations this treatment usually produces cure in three days.

Treatment with these drugs allows bacterial conjunctivitis to be settled much more rapidly than with earlier methods but, when they cannot be obtained, it should always be remembered that frequently repeated irrigations with normal saline will cure the majority of cases of conjunctivitis due to pyogenic infection.

The management of *allergic types of conjunctivitis* has been made easier by the use of the antihistamine group of drugs. Antistin-Privine is an example, and when used every four hours in such allergic manifestations of the conjunctiva as hay fever, it gives rapid relief; 1 per cent. ephedrine drops in normal saline are also useful.

Some cases of conjunctivitis tend to be recurrent and in these the effect of excessive dandruff and of nasopharyngeal infection should always be investigated. Refractive errors have been considered to be a factor in the incidence of *chronic conjunctivitis*, and they should be looked for, although it is doubtful if they are often of serious importance.

Conjunctivitis is not a painful disease, and in uncomplicated cases it does not result in deterioration of vision, but it causes discomfort, and requires energetic treatment. Particular care must be taken to ensure that treatment is not stopped too soon, or a recurrence may occur, due to organisms which are resistant to both groups of chemotherapeutic drugs, the treatment of which is neither easy nor satisfactory.

A. G. CROSS, M.D., F.R.C.S.

STAMMERING

In a typical stammer there is an interruption of speech flow by a moderate degree of spasm in one or more muscles, such as the diaphragm or muscles of the glottis, tongue or lips. It occurs in about 1 per cent. of people, is about five times more common in the male, and generally starts between the age of three and six years. At a later age its onset is often associated with mental strain, as in war time.

The patient may react to the spasm by forceful muscular movements, so that secondary symptoms supervene, such as jerking of the shoulders or severe facial contortions. Symptoms vary in degree in different patients, from the slight stammer evoked by excitement or hurry to almost total hold-up of speech.

Recent studies show that the stammer occurs chiefly in the first three words of a sentence and in adjectives, nouns, adverbs, verbs and long words (Brown, 1945). Most affected children have periods of relative intermission, as when they are

troublesome, small doses of ephedrine by the mouth or "elixir ephedrine co." (Parke, Davis) are useful. The complications, such as otitis media and sinusitis, usually occur about the tenth day. If the patient has not recovered in ten days, search is made for any complication.

PROPHYLAXIS

Prophylaxis, or the prevention of infection is of importance to the many children, young adults and the tuberculous who are peculiarly susceptible to colds. The incubation period of colds is about twenty-four to forty-eight hours, but for how long catarrhal patients are infective is not known. It is presumed that while patients have a raised temperature they are infective, and isolation, if enforced, should be continued for two days after the temperature is normal. Isolation is often impracticable and too expensive in personal restrictions to receive general adoption. However, isolation could be enforced in schools. The infection is air-borne and droplet infection is common. Polluted milk, water, food, feeding utensils, or the carrier patient may be a source of infection; the swimming bath before the introduction of the modern hygienic bath was a source of infection. The daily use of sprays, nasal lotions and gargles has been advocated by some, but clear evidence that they are of any benefit is lacking and some observers consider them to be more harmful than beneficial.

The increase of the resistance and of the immunity of the individual is promoted by careful hygiene, improvement in surroundings, and good food. The value of anti-catarrhal vaccines and of sunlight is disputed, although some cases have benefited by such treatment.

E. D. D. DAVIS, F.R.C.S.

CONJUNCTIVITIS

INFLAMMATORY conditions of the conjunctiva occur very commonly in human beings and are due, predominantly, to bacterial and allergic causes. They may appear in acute form or run a long and chronic course. Usually the lesion is isolated, but it may be associated with blepharitis or keratitis, especially if due to a staphylococcal infection. Epidemic kerato-conjunctivitis, probably a virus infection, is also a condition in which the conjunctiva and cornea are affected together. Reiter's disease, in which conjunctivitis, arthritis, and urethritis are associated, is a syndrome of doubtful etiology, for which treatment is difficult.

TREATMENT

The treatment of bacterial conjunctivitis has been revolutionized by the development of penicillin and of the drugs of the sulphonamide group.

Penicillin drops, made up in a strength of 2,500 Oxford units to the cubic centimetre and instilled into the eye every two hours, have a rapidly curative effect on the common forms of conjunctivitis due to the pyogenic cocci, unless the strain is penicillin resistant. Penicillin can also be used in the form of an ointment, which may be more convenient. Rapid improvement should occur and the pathological condition should have settled almost completely in three days. It must be emphasized that if penicillin be employed it must be ordered in full dosage, or there is a risk that penicillin-resistant strains may be developed; and treatment should continue for some days after clinical cure has occurred, to safeguard possible recurrence. It should also be pointed out that a small proportion of patients are sensitive to penicillin, and that they develop marked irritation of the eye with swelling of the lids when the drug is employed. This must be regarded as an indication for the employment of other treatment.

The sulphonamide group of drugs is also useful in the treatment of conjunctivitis, although there is some controversy regarding the precise indications. There is some evidence that the sulphonamides are most helpful in the virus conjunctival in-

courses or to unqualified persons who rely on some of the various tricks or dodges for temporarily liberating speech.

The London County Council, however, has had centres for stammerers since 1917, and Boome (1938) relies to a large extent on relaxation exercises in the initial stages of treatment. The same authority has also shown how much could be done for mentally defective stammerers. There is, however, an advantage in having the patient treated at a hospital which combines a speech clinic with a psychiatric and child guidance department. There should, of course, be the closest liaison between them.

The technique of *speech therapy* is admirably described by Miss Kingdon-Ward (1941) of the West London Hospital. The main points are teaching the patient how to relax, both in a general way and also in relation to the voice spasm. The patient is encouraged to seek out those situations in which he speaks naturally and with most ease. Various practical hints are given. The approach is continually varied and the patient's interest sustained. She warns against such artificial aids as "taking a deep breath first", "stopping and thinking", substituting easier words or developing "will-power and determination". The usual schedule is followed in the child guidance department which the child also attends. Parents are interviewed and, if necessary, the school authorities as well. There are mental tests and attempts are made to liberate constructive activity. There is interpretation of play therapy, and so on.

When *adults* are concerned the psychiatric approach is the same in principle as that used in other functional disorders. With stammerers, however, there are special features in therapy which require mention. The practitioner adopts a friendly, confident and matter-of-fact attitude towards the patient. In the over-tense cases, narcosis with pentothal or trilene helps relaxation and enables further exploration of the mind. Hypnosis is an excellent method of inducing relaxation, especially if a stroboscopic lamp is used. The patient in time looks on the vocal spasm as something external to himself to be dealt with unemotionally.

When a stammer has followed a *psychic trauma*, abreaction has occasionally relieved the symptom, thus hastening ultimate recovery. Handedness should be tested, but I have had only one case in which it was an important causal factor. After, as it were, getting inside the patient's mind and so understanding his conflicts, suggestion can be used to break the habit. One concentrates on the sensations which the patient experiences when talking well, and also on the new calm outlook which he is acquiring. As he becomes more confident he discards his old tricks of speaking unnaturally or of dodging words of which he is afraid. Although such active methods carried out over a comparatively short period may greatly improve the condition, it may be a long time before the trouble is entirely mastered, and continued attendance at the clinic is therefore advisable, as even in the most severe cases recovery can ultimately occur.

A. SPENCER PATERSON, M.D., M.R.C.P., DIPL. PSYCH.

References

- Boome, E. J., and Richardson, M. A. (1938): "Relaxation in Everyday Life," London.
 Brown, S. F. (1945): *J. Speech Disord.*, **10**, 181.
 Despert, G. Louise (1946): *Amer. J. Orthopsychiat.*, **16**, 100.
 Hahn, E. F. (1943): "Stuttering," California.
 Kingdon-Ward, Winifred (1941) "Stammering," London.
 Kopp, H. (1946): *Amer. J. Orthopsychiat.*, **16**, 1, 114.
 Maas, O. (1946): *J. ment. Sci.*, **92**, 357.
 Nelson, S., Hunter, N., and Walter, U. (1945): *J. Speech Disord.*, **10**, 335.
 Seemann, M. (1935): "Verhandlungen des VI Kongresses der Internationalen Gesellschaft für Logopädie und Phoniatrie," Vienna.
 Stein, L. (1937): "Sprach- und Stimmstörungen und ihre Behandlung," Leipzig and Vienna.

relaxed or talking to congenial companions. Conditions under which speech may be freed are:—

(1) When cortical control is relaxed, e.g., under a narcotic, talking in sleep, hypnosis, delirium, or immediate experience of strong emotion, as in swearing or when laughing or joking.

(2) When speech is different from usual, e.g. singing, whispering, screaming.

(3) When fear is temporarily in abeyance through manipulation (Rivers), i.e., carrying out some voluntary movement as when having a pebble under the tongue or holding one foot just above the ground.

(4) Introduction of rhythm, as in dancing, or with accompanying gestures, or beating time.

The trouble often lasts indefinitely if untreated, but it sometimes does clear up on its own. In severe cases, however, the distress suffered has even led to suicide.

ETIOLOGY AND PATHOLOGY

Heredity.—Stammering is a functional nervous disorder in which the relative importance of the constitutional predisposition varies greatly from case to case. It is often found to have occurred in previous generations. A recent investigation shows it to be more common in twins than in others. Twin studies would seem to emphasize also the inherited factor, for in 10 uni-ovular twin pairs when one twin was affected, in 9 cases the other was also. Of 30 pairs of binovular twins, however, when one stammered, in only two pairs were both affected (Nelson *et al.*, 1945). This would seem to show that the fact of identical heredity is more important than similar environment.

Muscular incoordination.—At one time great stress was laid on latent left-handedness and on "crossed laterality", i.e. left-handed and right-eyed, or *vice versa*. (To test "eyedness" one closes one's left eye and asks the patient to point with a straight arm at one's open eye. If the patient's hand is under his left eye, he is left-eyed). Although this aspect is occasionally important, recent studies have been directed more to testing general muscular coordination. Kopp (1946) has reported a deficiency in fine motor coordination and manual skill (including writing); also large motor coordinations were grossly abnormal, although a few stammerers were good at games. Their verbal ability, however, was rather above average.

Psychological factors.—Some writers have mentioned physical abnormalities, brain lesions following whooping-cough or injuries, and abnormal vascular reflexes (Stein, 1937; Seemann, 1935; Maas, 1946). In many cases, however, family history and physical examination are negative. The important factor, as first pointed out by Crichton Miller in 1912, is psychological. In the typical stammerer, obsessional traits are present to a greater or less degree. He has a rigid personality and indifferent ideas are unduly loaded with emotion. Patients are tense, and some feel sure that a particular word about to be used will cause stammer, and they are therefore always seeking synonyms. Psycho-analytical theory associates an obsessional make-up with undue preoccupation with mouth and anus in infancy, and Despert (1946) found some corroboration of this in case histories in which acquisition of toilet habits was associated with coercive or punitive measures. Thumb-sucking and nail-biting were common. The same mental mechanisms may occur in stammerers as in other cases of functional nervous disorder, e.g., an unconscious retreat from the world. Stammering is a frequent symptom in cases of compensation neurosis.

TREATMENT

Since stammering may occur in many different types of case there can be no universal or quick-acting remedy. One book (Hahn, 1943) describes the theories and therapeutic measures of 25 different authorities. Many patients resort to correspondence

Cheilitis glandularis is a condition in which mucus exudes from dilated orifices of mucous glands causing the lips to stick together and eventually to become enlarged. Actinic cheilitis from sun exposure, sensitivity to mouth washes, dentures and fruit juices should be excluded. Alternative differential diagnoses are lupus erythematosus, and erythema multiforme of chronic type confined to the lips and mucous membranes of the mouth.

Small doses of sulphonamide, one tablet twice daily, for some weeks might improve the condition. Ascorbic acid should be given as a routine during this sulphonamide therapy, and might even help in massive doses by mouth and parenterally. White cell counts would also be required.

GEOFFREY HODGSON, M.B.E., M.D.

Greying of the Hair in Women

QUERY.—Are there any measures which are effective in delaying premature greying of the hair in women? I am particularly interested in the use of para-amino-benzoic acid for the purpose.

REPLY.—Greyiness of the hair, even in women, cannot truly be described as premature unless it begins to appear in the twenties or early thirties. Sometimes the hair returns to its original colour following treatment of associated general ill-health or disease of the scalp. External factors, such as washing the hair with alkalis or too much sunlight, play a part. Grey hair and alopecia have been reported in children suffering from nutritional deficiencies and the condition is said to have improved more rapidly when biotin was given than when nicotinic acid, thiamine and other vitamins were tried; the trials were not very carefully controlled. Pantothenic acid will restore from grey to black the hair of rats previously on a diet deficient in this vitamin. Work on para-amino-benzoic acid (the anti-grey-hair factor) has not been substantiated. Therefore if there is nothing to treat such as general ill-health or scalp disease, the patient must learn to grow old gracefully or resort to dyes and their dangers.

DAVID I. WILLIAMS, M.D., M.R.C.P.

Vitamin E in Angina Pectoris and Coronary Thrombosis

QUERY.—Can you give me any information on the use of vitamin E in massive doses in cases of coronary thrombosis and angina pectoris?

REPLY.—It is now recognized that vitamin E has an influence on metabolism and nutrition of muscle and nerves in addition to its earlier

known effect on reproduction. When a brown fluorescent pigment was found in the cardiac muscle as well as in the skeletal muscles in E-deficient animals, interest in the possible effect of vitamin E in heart disease arose. Vogelsang and Shute (1946) claimed that vitamin E was of clinical value: "Its effect upon patients having congestive heart disease and the anginal syndrome is marked; it increases exercise tolerance and diminishes or abolishes anginal pain during the period of administration; its diuretic effect is pronounced". This observation has not been confirmed, and Makinson, Olesky and Stone (1948) tested vitamin E in twenty-two patients with typical angina of effort, comparing its effect with that of other drugs. They concluded that it is not of any therapeutic value in the routine treatment of angina pectoris. One patient complained of a dry feeling in the throat, two had increased headache, and one noted pronounced vasodilatory effects in the form of flushing of the face, throbbing headaches, and giddiness. A possible deleterious effect of vitamin E is increased deposition of cholesterol in the aorta. Bruger (1945) observed this in rabbits but evidence for or against this happening in man is not available.

There is no place for vitamin E in the therapeutics of coronary heart disease in man.

References

- Bruger, M. (1945): *Proc. Soc. exp. Biol. N.Y.*, 59, 56.
Vogelsang, A., and Shute, V. (1946): *Nature*, 157, 772.
Makinson, D. H., Olesky, S., and Stone, R. V. (1948): *Lancet*, 1, 102.

C. J. GAVEY, M.D., F.R.C.P.

The Health Act and the Services

QUERY.—I have recently been consulted by a senior Colonial officer at present on leave in this country. He is anxious to know what his position will be under the new National Health Act. Will he be entitled to "free" medical service, and if so, what is the procedure?

REPLY.—The general principle is that every man, woman, and child in this country is entitled to free medical attention under the Service. If a Colonial officer is on short leave he should apply to the doctor of his choice to be treated as a temporary resident (provided of course that the doctor has joined the Service). If he is likely to be in the country for a considerable time, for example, six months, it would be better for him to apply to join a doctor's list in the usual way. He is, of course, entitled to all the benefits of the hospital and specialist service and, indeed, of all parts of the National Health Service.

LESLIE BANKS, M.D., F.R.C.P., D.P.H.

NOTES AND QUERIES

Recurrent Boils

QUERY.—A male patient aged forty-five years has been suffering from septic spots and small boils (recurring) on his face and neck for the past six to seven years. I have given him penicillin injections, 200,000 units morning and evening for ten days. Previous to this he had a course of sulphamezathine. His blood sugar (fasting) is 108 mgm. per 100 c.cm. His condition is more or less the same. Some years ago he had an autogenous vaccine prepared, also treatment by ultra-violet light and X-rays. He has no obvious focus of infection. I shall be grateful for any suggestions on treatment.

REPLY.—It is suggested that a glucose-tolerance test be made, particularly as the fasting blood-sugar is on the high side. If the *average* figure for the half-hourly estimations is above 120 mgm. per cent. it may be assumed that there is some degree of sugar intolerance. There is evidence that the amount of sugar in the skin may be excessive, although the blood sugar curve be within normal limits (Urbach's "cutaneous glycohistiemia"). Exact details of the patient's usual diet should be obtained, particularly as regards his intake of sugar, sweets, cake, jam, starchy foods, and *alcoholic drinks*. There should obviously be a correlation between the carbohydrate intake and the amount of physical exercise taken.

Cases of this kind usually respond well to a relatively high protein dietary with plenty of green vegetables and fresh fruit, and restriction of sweet and starchy foods. Starchy foods should, so far as possible, be restricted to those containing vitamin B₁. A high carbohydrate dietary, particularly with an excessive fluid intake (beer and tea drinkers) certainly favours infection both of the skin and mucous membranes. The diet should be supplemented with the whole vitamin B complex (standardized yeast tablets, marmite, liver-and-yeast concentrate) and, when fruit is scarce, ascorbic acid.

Although it is stated that there is no obvious focus of infection it is imperative to exclude the presence of apically infected teeth and of residual infection in the alveolar margins of edentulous portions of the jaws, since there seems to be more than a coincidental association between dental infection and boils chiefly localized to the head and neck.

Local measures.—The addition of zinc sulphate to the daily bath and to the water used for washing the face, head, and neck is advisable. It should be dispensed in $\frac{1}{4}$ lb. packets, the contents of one packet being added to the

bath. The areas on which the boils tend to occur should be sponged every night with

Weak tincture of iodine B.P. . . 1:0
Industrial methylated spirit . . to 10:0

unless the patient's skin is sensitive to iodine. The skin should then be dusted with a borated talc powder.

Vaccine therapy.—I am satisfied that in chronic staphylococcal infections of the skin, vaccine therapy by *intra*dermal injection is more effective than by the more usual subcutaneous route.

H. W. BARBER, M.B., F.R.C.P.

Cheilitis Exfoliativa

QUERY (from India).—One of my patients, aged twenty-six, has been suffering from an intractable cheiliosis exfoliativa for the last two years. There is weeping and crusting along the lips resulting in painful raw surface when the crusts come off. It was thought to be due to a new brand of lipstick she had recently changed to. She has stopped using lipstick entirely. Constitutionally she is perfectly healthy. No improvement has resulted from local application of gentian violet, silver nitrate and resorcin, penicillin ointment, some 100 injections of vitamin B complex, 25 of riboflavin, 25 of calcium and about 25 liver extract injections. All possible allergic substances, such as face powder, rouge, creams, and various food articles have been eliminated without avail. She has now been advised ultra-violet irradiation and deep X-ray therapy as a last resort. The trouble has restricted her social life considerably and is having some effect on her mental outlook also. I shall be grateful to have details of possible lines of treatment. What do you think is the causative agent?

REPLY.—The fact that the condition of the lips has not improved when the use of lipstick, and presumably all other lip salves, was stopped makes it unlikely that a cosmetic could be the causative factor. Nail polish will, however, occasionally cause cheilitis. The description fits cheilitis exfoliativa which commonly occurs in young women. A neurotic habit of picking or licking the lips may aggravate the disability. It is a chronic condition and the cause is not known. It is usually resistant to treatment, but fractional doses of X-rays, 50 r to 80 r with low Kv may be tried weekly for four doses. Ultra-violet light might aggravate. Locally, 1 per cent. ammoniated mercury in an emulsion base may suit. Sulphur ointment is recommended by some.

this must be controlled by penicillin eye-drops (2,500 units of crystalline penicillin per c.cm.) before the course of subconjunctival injections is instituted.

Oral Myanesin in Spastic Conditions

THE use of myanesin (3-ortho-toloxyl-1,2-propanediol) by the oral route in a series of spastic and hyperkinetic disorders is recorded by F. M. Berger and R. P. Schwartz (*Journal of the American Medical Association*, June 26, 1948, 137, 772). The drug was given as a 3.3 per cent. (weight in volume) solution in 20 per cent. (volume in volume) aqueous propylene glycol, with syrup of cherry 20 per cent. (volume in volume) to improve the taste of the mixture. The usual single dose was 30 c.cm. of the mixture (1 gm. of myanesin), with proportionately smaller doses to children, the number of doses daily depending upon the individual requirements. In hemiplegic patients in whom paralysis had been stationary for four to seven years there was a striking recovery of the voluntary movements of the paralysed limbs ten to twenty minutes after administration of the drug, the maximum benefit being obtained after two to three days' medication, and thereafter maintained by 1 gm. doses in the mixture, three to five times daily. Good results were also obtained in some cases of cerebral diplegia, and in Parkinson's syndrome there was reduction of tremor and rigidity. The effect of the oral administration of the drug in this latter condition was not as spectacular as with parenteral administration, but the duration of the action was longer and there were no undesirable side-effects. Relief of both spasm and pain was obtained in various conditions causing muscular spasm—arthritis of the cervical spine, subacromial bursitis, low back pain, and osteoarthritis of the hip. Side-effects from the oral administration of myanesin were rare: neither blood pressure, heart rate nor respiration were affected, and examination of the blood for hæmoglobinæmia, and of the urine for protein and blood, gave negative results. The only side-effects noted were anorexia in 1 out of 59 patients treated and a transient feeling of lassitude in several cases. Nevertheless, it is pointed out that "patients receiving the drug should . . . be watched closely, as the chronic effects . . . on human beings are still unknown".

Picrotoxin in the Treatment of Barbiturate Coma

TEN cases of severe barbiturate intoxication, with typical coma, have been treated with picrotoxin by A. I. Suchett-Kaye (*Presse Médicale*, July 10, 1948, 56, 495). The solution

employed was that prepared by Abbott Laboratories, 1 c.cm. of which is stated to equal 3 mgm. of the active substance. The dosage varied with the individual case:—In one case, a woman who had taken 6.5 gm. medinal and was in a state of deep coma, after washing out of the stomach and lumbar puncture, was given three intravenous injections of 12 mgm. (4 c.cm.) at fifteen minute intervals, followed by intramuscular injections of 6 mgm. (2 c.cm.) every quarter of an hour. After the sixty-sixth injection (total amount of picrotoxin 414 mgm.) the patient began to come out of the coma and the drug was stopped. In another case in which the patient had taken 2.5 gm. nembutal and was in deep coma, intravenous injections of 6 mgm. were given, and after the seventh injection consciousness was regained.

It is stated that in order to be effective picrotoxin administration should be started in sufficient dosage as soon as possible after diagnosis is confirmed, and administration must be continued, sometimes for days, by injections at fifteen- to twenty-minute intervals, intravenously or intramuscularly according to the severity of the case. The treatment is stopped when spontaneous movements return and the patient shows signs of coming out of the coma. If there is a recurrence of symptoms the injections must be resumed. Should convulsions occur, an intravenous injection of a short-acting barbiturate, for example nembutal, should be given in dosage of 0.1 to 0.2 gm. Adjuvant measures are (1) lavage of the stomach, which, apart from its therapeutic value, should be carried out in order to confirm the diagnosis; (2) rehydration by means of glucose and saline solutions, by subcutaneous, rectal or gastric route; (3) oxygen therapy; (4) chemotherapy—penicillin for choice, especially in the stage of coma; later, sulphonamides can be prescribed for pulmonary complications; (5) cardio-respiratory analeptics.

Home Hydrotherapy for Relief of Tension

"HOME hydrotherapy", according to J. R. Gay (*Proceedings of the Staff Meetings of the Mayo Clinic*, April 14, 1948, 23, 193), "is a useful means of attacking disturbing sensations of tension, sensory and motor hyperactivity and mild visceral dysfunctions. It is safer and often more effective than prolonged sedation with derivatives of barbituric acid." The recommended procedure is as follows:—An ordinary bath tub is filled three-quarters full with water at exactly 98° F. (36.7° C.) (a bath thermometer must be used). The patient lies back in the bath so that only his head is above water. The

PRACTICAL NOTES

Sulphathalidine in Urinary Tract Infections

THE results obtained in 47 cases of infection of the urinary tract, as a complication of gynaecological surgical procedures or of pregnancy, by the use of sulphathalidine (phthalylsulphathiazole) are recorded by C. Gordon Johnson, L. H. Lorenzen, and R. Y. Mayne (*American Journal of Obstetrics and Gynecology*, July 1948, 56, 160). In all cases diagnosis was confirmed by culture, the first being made before the beginning of treatment and repeated at the end of the first week's treatment, and then weekly until negative. The routine dosage adopted was 6 gm. daily (approximately 0.1 gm. per kgm. body weight), in divided doses four-hourly for the period of hospitalization (approximately 1 week), and then 4 gm. daily for the period of treatment. Eight patients received only 2 or 3 gm. daily. The total dosage for each patient varied from 27 to 86 gm.—average 53 gm. Of the 47 cases the organism involved in 27 was *Esch. coli*, and in 26 cure was obtained both symptomatically and bacteriologically. In 50 per cent. negative cultures were obtained in one week or less, and in 77 per cent. in two weeks or less. The drug had little effect on cystitis caused by *Aerobacter aerogenes* or *Alkaligenes faecalis*, but did have some effect on urinary tract infections due to staphylococci and streptococci. In conclusion it is stated that because of its poor absorption and low toxicity sulphathalidine can be used when other sulphonamides would be contraindicated and "this is especially true in pregnancies complicated by impaired kidney function or severe anaemia". The dosage necessary to bring about cure was 0.1 gm. per kgm. body weight daily, for an average of two weeks. In eight cases the dosage used was 0.05 gm. per kgm. body weight.

Penicillin in Diphtheria and Diphtheria Carriers

FORTY-FIVE cases of acute diphtheria were treated with penicillin during a six-month period by J. D. Crawford (*New England Journal of Medicine*, August 5, 1948, 239, 220). All the patients received an initial course of penicillin of 50 doses of 20,000 units each, in some cases a larger dosage being given for the first three days: 80 per cent. showed negative cultures after treatment. At the beginning of the author's study twenty carriers, all asymptomatic convalescents who had been hospitalized for six weeks or more and whose nasopharyngeal cultures were persistently positive for virulent

diphtheria bacilli, were treated with penicillin:—Five patients were treated locally with sprays of penicillin solution containing 500 units per c.cm.; seven were treated with 1,000,000 units of penicillin intramuscularly, 40,000 units being given three-hourly for twenty-five doses; eight were treated parenterally with 20,000 units three-hourly for fifty injections. The best results were obtained in the last group (20,000 units three-hourly for fifty doses), of which 87 per cent. were negative after treatment. In the group receiving local sprays one patient alone (20 per cent.) was negative after treatment, and in the group receiving 40,000 units for 25 doses the negative culture rate was only 28 per cent. A further study of 52 chronic carriers, 44 of whom were treated by injection of 20,000 units of penicillin three-hourly for fifty doses, showed a negative culture rate of 87 per cent. On the basis of the results obtained it is stated that "penicillin is a valuable adjunct in the treatment of diphtheria and the diphtheria carrier state, but . . . it does not supplant the use of antitoxin in the acute stage or obviate the necessity for surgery in a selected group of carriers".

Penicillin and Corneal Ulcers

As a result of his experience with 26 cases, Kamel Rizk (*British Journal of Ophthalmology*, August 1948, 32, 497) recommends the following treatment for severely infected corneal ulcers:—The eye is first anesthetized with two instillations of 1 per cent. pantocaine solution at three-minute intervals. The solution of penicillin is prepared by adding 5 c.cm. of a 1 per cent. novocaine solution in distilled non-pyrogenic water to a bottle of 100,000 units of crystalline penicillin. Novocain is used for this purpose in order to reduce the pain caused by the infiltration of fluid under the conjunctiva. The eye is then opened and fixed by a pair of Desmarres' retractors, and 0.5 c.cm. of the penicillin solution is injected subconjunctivally at a distance of 2 to 3 mm. from the limbus. The injections are given twice daily for five days. Unless the eyes are predisposed to glaucoma, 1 per cent. atropine ointment is also applied twice daily. After the course of penicillin injections is completed, treatment is continued with frequent wash and hot fomentations. In most cases the progress of the ulcer is arrested after the first injection. In those cases which did not respond well to the first few injections, treatment was supplemented by frequent wash, hot fomentations and the local application of sulphadiazine ointment twice daily. Should there be a mucopurulent or purulent discharge,

children showed that 36 used swimming baths all the year round; 15 during the summer months only; 39 used shower baths regularly after physical training, and in only 2 cases had communal gym shoes been worn. Prevention was limited to the exclusion of established cases from places which favoured spread, such as swimming baths and showers, and stress was laid on the wearing of properly fitted, and comfortable shoes; this latter because in many cases abrasions, which provided a primary stimulus to infection, were present. Treatment consisted in swabbing the whole foot with surgical spirit; removal of callous tissue; painting the area surrounding the wart with collodion or tincture of benzoin; localization of the wart by means of a stockinette cover in which a hole, approximately the size of the wart, was cut, and through which chlorosal (salicylic acid 60 per cent., chloral hydrate 5 per cent.) was applied. A felt pad was then placed over the wart to prevent pressure, and the whole dressing enclosed in stockinette and secured with adhesive plaster. The patients were instructed to keep the dressings dry, and to return in seven to fourteen days for fresh dressing. In some cases monochloroacetic acid and silver nitrate were used instead of chlorosal. The average number of treatments required was three. A follow-up of 59 children who had completed their treatment

nine months previously showed that in no case had there been a recurrence.

Débridement of Necrotic Wounds

THE use of acid-containing preparations in the removal of necrotic tissue coagula in wounds was evolved by American workers during the 1939-45 war. The original base for these preparations was unsatisfactory. The problem of the base for such preparations has been investigated by R. E. M. Davies (*Pharmaceutical Journal* June 19, 1948, 160, 431) who recommends the following formula:—

Dilute phosphoric acid B.P.	5	per cent.
Glycerin	10	per cent.
Tylose M.50 or Cellofas WLD	6	per cent.
Chlorocresol	0.1	per cent.
Water	78	per cent.

Warm water containing the chlorocresol, glycerin and dilute phosphoric acid is poured on to the cellulose derivative. This mixture is allowed to stand, with frequent stirring, until a clear, colourless, homogeneous gel is formed.

Both tylose M.50, a brand of methyl cellulose, and cellofas WLD, a brand of methyl ethyl cellulose, are available in Great Britain. It is said that if this gel is made in bulk and care is taken not to incorporate air-bubbles, it can be stored in full, air-tight containers until required. Over a period of months no change has been noted in the pH.

REVIEWS OF BOOKS

The Training of a Doctor. London: Butterworth & Co. (Publishers), Ltd., 1948. Pp. 151. Price 7s. 6d.

Medical Education. By FFRANGCON ROBERTS, M.D. London: H. K. Lewis & Co., Ltd., 1948. Pp. xv and 172. Price 12s. 6d.

The Clinical Apprentice. By JOHN M. NAISH, M.D., M.R.C.P., and JOHN APLEY, M.D., M.R.C.P. Bristol: John Wright & Sons, Ltd., 1948. Pp. x and 200. Figures 71. Price 15s.

If the medical curriculum is not all that it should be, it is certainly not for lack of writings on the subject. Whilst the cynic may talk glibly about the inverse ratio between the amount of writing and the amount of action, the more level-headed members of the profession must feel that this intense interest in a major problem is a healthy sign, and that, if only by a slow process of attrition, the day must be approaching when action will at last be taken. The three books reviewed here are an interesting cross-section of the various approaches to the problem.

The Training of a Doctor is the report of the medical curriculum committee of the British Medical Association which was set up in 1945, under the chairmanship of Professor Henry Cohen of Liverpool. It submits the whole of the medical curriculum to careful scrutiny and presents a most detailed scheme to replace the present one. Whilst there will be a general welcome for the insistence upon the evils of premature specialization at school, one serious criticism of the report is the tendency to treat the training of a doctor as a technological procedure rather than as a cultural one. With the general outline of training there will be little disagreement, but it is rather an anticlimax to find that one of the major conclusions is the necessity for the setting up of an Association of Teachers in Medical Schools. Surely this is isolationism in its worst form. The members of the committee, however, are to be congratulated upon the care and skill with which they have carried out their main task, and they can rest assured that whenever reform is at last carried out, their labours will not have been in vain.

Dr. Ffrangcon Roberts's book on *Medical*

minimal stay in the bath is twenty minutes, and should the patient stay for longer the temperature of the water must be adjusted to 98° F. every twenty minutes by the addition of warm water. The usual course of events is a slight chill on entering the water. This is followed by a warm subjective sensation and a comfortable sense of fatigue. In some cases the patient may become so drowsy that he falls asleep. If the patient is not going to bed following the bath, then he should follow it by a cold sponge bath or shower. The baths should be taken at the time of day when tension is maximum, and this must be carefully determined by the practitioner. Should this occur in the evenings, then the bath immediately before retiring for the night is often an excellent sedative.

The Treatment of Papillomas of the Bladder with Podophyllin

A PRELIMINARY report of the value of podophyllin in the treatment of papilloma of the bladder is given by J. E. Semple (*British Medical Journal*, June 26, 1948, i, 1235). The report concerns four cases, in all of which after treatment with podophyllin, perurethral fulguration was rendered possible: without this preliminary treatment cystotomy and open fulguration would have been necessary in three of the cases. The method adopted is as follows:—

Following diagnostic cystoscopy the window of the cystoscope is placed immediately over the growth and the bladder emptied: 3 c.cm. of 0.5 to 1 per cent. podophyllin in liquid paraffin is introduced into the bladder through the instrument. The patient is turned on to the side on which the growth is situated and left lying for half an hour, thus allowing urine to collect in the bladder and float the oil off the tumour. The patient is then turned on to the opposite side to maintain contact of the suspension with the papilloma, and encouraged to empty his bladder when the urge arises, thus expelling the podophyllin. If no reaction occurs, then 5 c.cm. of 4 per cent. podophyllin in liquid paraffin is introduced through the cystoscope four to seven days later, the same procedure being carried out. A third application, using 5 c.cm. of 8 per cent. podophyllin in liquid paraffin, is made a week later. Depending upon the size and extent of the growth further applications can be made.

It is stated that the number of cases treated was too small to warrant definite conclusions, but the results would appear to indicate a further trial with podophyllin and drugs with allied action.

β-Diethylaminoethyl Dehydrocholate in Fibrositis

THE use of β-diethylaminoethyl dehydrocholate (S.42:Roche) in 200 cases of primary fibrositis is recorded by D. Roden and F. Wrigley (*Irish Journal of Medical Science*, July 1948, 6th series, No. 271, p. 330). The 200 cases were divided into three groups: (1) 100 cases of primary fibrositis were given subcutaneous or

intramuscular injections of 5 mgm., the number of injections varying from 5 to 20, and given daily, or at intervals of two, three or more days. In 28 cases there was disappearance of symptoms after treatment, in 24 marked improvement, in 20 some improvement, and in 28 no change. The second group consisted of 50 cases of acute fibrositis (acute torticollis, lumbago, tenosynovitis and bursitis). They received daily injections of 5 mgm. S.42; 40 became symptom-free and in 10 there was no change. In the third series, which comprised 50 cases of subacromial bursitis, the patients were given 5 mgm. S.42 every third day until 12 injections had been given. Relief was obtained in 14, but no patient had normal range of movement before the injections were discontinued.

Tyrothricin for Diphtheria Carriers

TYROTHRIN is one of the most useful means of sterilizing diphtheria carriers, according to G. Polistina (*Minerva Medica*, August 11, 1948, 39, 125). He treated 11 carriers and 23 convalescent patients, using a pharyngeal spray of 10 c.cm. aqueous solution containing 50 mgm. per cent. tyrothricin, and nasal instillation of a water and propylene glycol, or a water and glycerin solution of 4 mgm. per c.cm., repeated at equal intervals three times a day for six to eight consecutive days. In babies, instead of using a spray, he painted the pharynx with the same solution as for nasal instillation. In some resistant cases he combined spraying with painting the pharynx. As soon as cultures for *C. diphtheriae* were negative, treatment was discontinued. Patients were considered sterile if 3 cultures made at 7-day intervals were negative. Tyrothricin had an antibacterial effect not only on *C. diphtheriae* but also on all the common flora of the nasopharynx. In the carriers good results were obtained in 10 out of 11 cases (91 per cent.). In the convalescent cases sterile cultures resulted within twelve days in 14 of 23 cases, or 60.85 per cent. (successful), and on the fourteenth day in 3 cases, or 13.04 per cent. (partially successful). The results in 3 cases (13.04 per cent.) were inconclusive as cultures were not sterile until after the sixteenth day and the possibility of a spontaneous cure could not be excluded. Four cases were resistant to treatment—1 carrier and 3 convalescents.

Plantar Warts

CAUSAL factors, preventive measures, treatment and the results obtained thereby are discussed by M. Watkins (*Chiropodist*, July 1948, 3, 173) in a review of 150 cases of plantar warts occurring among school children. Inquiries as to the possible source of infection in 59 of the

examined. This is followed by an outline of the work of the Institute of Social Medicine in Oxford. "The meaning of normal and the measurement of health" is a masterly survey of an important but neglected subject, written in a stimulating style which is in contrast to the plebeian treatment of the relationship of social medicine to population problems. The final chapter, however, shows the author at his best when he discusses medical ethics and the new humanism. There may be some who will find it difficult to accept some of the conclusions, but no one who values the high ethical standards of the medical profession will fail to be moved by the warmth and skill with which these standards are here expounded.

Radon: Its Technique and Use. By W. A. JENNINGS, B.Sc., A.Inst.P., and S. RUSS, C.B.E., D.Sc., F.Inst.P. London: John Murray, 1948. Pp. x and 222. Figures 49 and 14 plates. Price 18s.

THIS useful book gives a full and detailed description of the preparation and use of radon. Part I is general in character and describes the disintegration of radio-active substances, the production of radon and its uses in medicine, biology and industry. Part II is intended mainly for the radon technician and gives a clear account of the types of radon containers used, their preparation from a typical radon extraction plant, and their measurement by ionization methods. The chapter dealing with the variation in activity within a group of seeds is of importance also to users of radon seeds. Part III, which deals with radon in medicine, describes the various methods used to obtain uniform dosage in γ -ray therapy. A device of particular interest is the so-called radon seed-chain, consisting of several radon seeds threaded together, which can be used in effect as a flexible radon needle. The authors are to be congratulated on so competently achieving their aim to write a book of reference on radon.

NEW EDITIONS

MUCH new material has been added to *Recent Advances in Anaesthesia and Analgesia*, by C. Langton Hewer, M.B., B.S., M.R.C.P., D.A., in its sixth edition (J. & A. Churchill Ltd., 21s.): physeptone, a new analgesic; metopryl and isopryl, two new ethers; a new short-acting barbiturate, kemithal; new information on the prophylaxis and treatment of pulmonary embolism; electronarcosis; dry-heat sterilization of syringes—these are but a few of the subjects dealt with in the new edition.

Sterility and Impaired Fertility, by Cedric Lane-Roberts, C.V.O., M.D., F.R.C.S., F.R.C.O.G., Albert Sharman, M.D., Ph.D., M.R.C.O.G., Kenneth Walker, F.R.C.S., F.I.C.S., B. P. Wiesner, D.Sc., Ph.D., F.R.S.E., and Mary Barton, M.B., B.S., in its second edition (Hamish Hamilton Medical Books, 24s.) contains among many new additions sections on tubal insufflation in the diagnosis of sterility, the use of the sulphonamides and penicillin in the treatment of infections causing infertility, pregnancy tests, X-ray irradiation and diathermy, Sims's test, and hormone therapy. This work deals in expert manner with all aspects of its subject.

Treatment by Manipulation, by A. G. Timbrell Fisher, M.C., M.B., Ch.B., F.R.C.S., in its fifth edition (H. K. Lewis & Co., Ltd., 25s.) has been extended in many sections, and particularly in those dealing with the use of manipulation in rheumatic diseases. The author's work is an interesting exposition of the value of manipulation in the hands of an experienced surgeon, and it is to be hoped that his wish expressed in the preface, that the Ministry of Health may organize the treatment of rheumatism for the inclusion of manipulative therapy, may materialize. The new edition is well illustrated.

Clinical Toxicology, by Clinton H. Thienes, M.D., Ph.D., and Thomas J. Haley, Ph.D., in its second edition (Henry Kimpton, 22s. 6d.) would seem to be a useful addition to the practitioner's library. In addition to giving detailed descriptions of poisoning from drugs and other substances, with the toxic doses, etiology, signs and symptoms, and treatment, a section is devoted to the chemical diagnosis of poisoning, in which the different tests are described in detail.

Pharmacology, Therapeutics and Prescription Writing, by Walter A. Bastedo, M.D., Sc.D., F.A.C.P., in its fifth edition (W. B. Saunders Co., Ltd., 42s.) has been enriched by many new additions: the antibiotics, antihistamines, anti-convulsants, analeptics, curare, BAL, folic acid, and the anticoagulants are among the new drugs included, as also details of the modern treatment of shock, malaria, and the anæmias.

Minor Surgery, by R. J. McNeill Love, M.S., F.R.C.S., in its third edition (H. K. Lewis & Co., Ltd., 22s. 6d.) has been brought up to date in all sections. This work is too well known to call for detailed description, but mention should be made of a most useful section on the injection treatment of varicose veins, and an excellent chapter on anaesthetics.

Education is as stimulating as it is critical. Free from the inevitable inhibitions attached even to a semi-official committee, he has allowed his intense individualism free play. His thesis is best summarized in his own words: "It [reform] is a search for unity and synthesis, in a subject which has a natural tendency to disunity and dispersion, a search for the ideal combination of science and empiricism; above all a search for a solution which needs no periodic stimulation but which, being based on fundamental principles, automatically keeps itself alive". This is the humanistic approach to the problem—a much more difficult one these days than the synthetic approach of the mere technician, but, as many of us believe, the correct one. Even Dr. Roberts cannot free himself from the human frailty of bias, as is seen in his insistence upon the importance of physics as opposed to chemistry, but no one can be completely objective. As an antidote to the dead hand of officialdom this is a book which should be read by all who are interested in this important problem.

The Clinical Apprentice is what might be described as the young man's approach to the problem. Here is practice—not theory. In other words, an outline is provided of how the student should be introduced to the clinical period. When it is pointed out that the book has an enthusiastic foreword by Professor J. A. Ryle, there is little need to say more. Here is the practical application of *The Natural History of Disease*. There are several other excellent introductions to clinical medicine, but this one has the advantage of being more personal in its approach and less comprehensive. In attaining simplicity some loss of balance occurs, but with this book by him as a guide the student will find his transition from the pre-clinical to the clinical period considerably facilitated.

Acute Intestinal Obstruction. BY RODNEY SMITH, M.S., F.R.C.S. London: Edward Arnold & Co., 1948. Pp. xii and 259. Figures 101. Price 18s.

THE subject of this monograph is of the utmost importance to every practitioner and surgeon; moreover it is one on which the literature is overwhelming, contradictory and uncoordinated. Rodney Smith speaks with the authority of a research worker and a practical surgeon trained in the hard school of the forward surgery of war; further, he has an uncommon gift of writing clearly, forcefully, and attractively. His enthusiasm for some of the technical tricks of the dog-surgeon gives a hint that he is still on the ascending side of a brilliant career—but his judgment is mature. His methods of classifica-

tion where they differ from the traditional ones are an improvement. The pathology of intestinal obstruction is first reviewed and the great volume of experimental work is analysed critically. A helpful section on diagnosis follows, containing a chapter on radiological diagnosis by Dr. Eric Samuel. Treatment, in which the pre- and post-operative phases, and the decision whether and when to operate and how much to do are far more important than operative technique, is admirably discussed. The final section discusses individual types of intestinal obstruction. The illustrations throughout are exactly right, well chosen, well planned and well drawn; each is necessary, and each says exactly what it is meant to say. This is the best book that has been written on the subject and one of the most valuable surgical monographs that has appeared since the war.

Manual of Leprosy. BY ERNEST MUIR, C.M.G., C.I.E., M.D., F.R.C.S. Ed. Edinburgh: E. & S. Livingstone Ltd., 1948. Pp. viii and 208. Figures 70. Price 17s. 6d.

DR. MUIR has given us a book, which, although a mine of information, is a model manual. It contains all essential facts in a readable rather than synoptic form and opens the reader's eyes to the many problems of control and treatment. Classification follows the Rio Congress (1946), a not yet satisfactory compromise between clinical and pathological differentiation of antigenic action and reaction. The rôle of children in maintaining this smouldering scourge is stressed, and various forms of resistance discussed, together with the sections on allergy and the lepromin test. Treatment by hydronocarpus, the sulphones, and surgery is outlined and evaluated. The illustrations are well chosen and reproduced, a few in colour. Here are vast experience and wisdom made readily available. The book is among the tools which should help to finish the job of achieving the unconditional surrender of one of mankind's oldest enemies.

Changing Disciplines. By JOHN A. RYLE, M.D. London: Oxford University Press, 1948. Pp. x and 123. Figures 13. Price 12s. 6d.

WITH that mastery of the English language and gift of exposition which have always characterized his writings, the Professor of Social Medicine in the University of Oxford expounds in this little volume his views on "the history, method and motives of social pathology". After a preliminary chapter on "social pathology and the new age in medicine", there follows one in which the importance of social conditions in the etiology of disease is

INTRAVENOUS ANÆSTHESIA

By WILLIAM W. MUSHIN, M.B., B.S., D.A., F.F.A.R.C.S.

Director, Department of Anæsthetics, Welsh National School of Medicine, Cardiff.

ANYONE who can put a needle into a vein can administer an intravenous anæsthetic. It is as easy as that; a fact that has in no small way contributed to the enormous popularity and value of this method of anæsthesia. Therein, too, lies its greatest danger, for there is nothing to stop an overdose being administered other than the experience and knowledge of the administrator. When a patient is overdosed with an inhalation anæsthetic he stops breathing, and the further entry of anæsthetic into his body is thereby stopped. This is not so in the case of intravenous anæsthesia, for the injection may be continued with the same facility until, and even after, the patient is reduced to a corpse.

Intravenous anæsthesia nowadays means evipan or pentothal; drugs which have recently been given the official pharmacopœial names of hexobarbitone and thiopentone sodium, respectively. Thiopentone is the intravenous anæsthetic most commonly used, because of its greater potency and constancy of action, and this article is based on it. However, with the exception of doses and concentrations which specifically refer to thiopentone, all that follows may be applied equally well to hexobarbitone, with very little adaptation.

Intravenous anæsthesia is administered for a number of reasons. As a discipline for safety it is a good thing for the anæsthetist holding the charged syringe in his hand to pause a moment and make quite sure in his own mind the purpose of the injection he is about to make.

THIOPENTONE FOR INDUCTION OF ANÆSTHESIA

Perhaps the injection is being made before an inhalation anæsthetic, merely to put a patient to sleep with a prick in the arm rather than a mask on the face. Without question it does this in a superb manner. The miraculously rapid and smooth onset of unconsciousness would have amazed the pioneers of anæsthesia of a hundred years ago, used as they were to the turbulence of induction with nothing but ether. Nevertheless, wonderful though it is, if the injection is being given as an alternative to the face mask, there must be no question but that this intention is in conformity with the patient's wishes. To administer thiopentone for this purpose when the patient says "I dread any kind of injection" or "I hate the needle" is as stupid as applying a mask after he has stated "I don't mind what you do to me so long as you don't put a mask on my face". In the main, experience

NOTES AND PREPARATIONS

NEW PREPARATIONS

ETHIODAN B.D.H. (ethyl-*p*-iodophenylundecate) is a contrast medium prepared for myelography. It is issued in boxes of 3 ampoules of 3 c.cm. by the British Drug Houses Ltd., City Road, London, N.1. These manufacturers have also recently issued **RUTIN** B.D.H., a derivative of flavone, for use in the prevention and treatment of hæmorrhagic conditions. It is supplied in bottles of 100 tablets of 20 mgm. Literature on both preparations can be obtained on application to the manufacturers.

HETRAZAN diethylcarbamazine (1-diethylcarbamyl-4-methyl-piperazine) is a new anthelmintic which has been subjected to extensive trials in the treatment of filariasis. The manufacturers are the Lederle Laboratories Ltd., and particulars can be obtained from Cyanamid Products Ltd., Brettenham House, London, W.C.2.

PENICILLIN CHEWING GUM A. & H. has been prepared for use in the treatment of oral infections due to streptococci and Vincent's organisms. The manufacturers are Allen & Hanburys Ltd., Bethnal Green, London, E.2, who issue the gum in boxes of 6 pieces, each containing 5000 units of penicillin, price 4s. 6d. per box.

STREPTOMYCIN-PENICILLIN CHART
A STREPTOMYCIN-PENICILLIN G chart which gives the clinical indications, details of the preparation of solutions, methods of administration and dosage of streptomycin calcium chloride complex and crystalline penicillin G, in different clinical conditions, has been compiled by Merck & Co. Practitioners in any country who desire a copy should write direct to Merck & Co., Inc., 161 Avenue of the Americas, New York, U.S.A.

NEW APPARATUS

RHEUMALON is a compact, portable apparatus devised for the use of electrotherapy in the home. It comprises a battery with indicator and leads, and a special solution (sodium chloride 13.7 per cent., hamamelis 0.015 per cent., calamine 0.009 per cent., mercurochrome 0.229 per cent., aqua pura 86.047 per cent.), all contained in a specially fitted case. The manufacturers are H. R. Shaw Ltd., Hints, Tamworth, Staffs, by whom Rheumalon is supplied complete with solution, price £12 12s., or the apparatus can be hired for a period of one month for £4 4s. Further particulars can be obtained from the manufacturers.

INTERNATIONAL SCIENTIFIC FILM CONGRESS

IN connexion with the International Scientific Film Congress which will be held in London from October 8 to 12, 1948, the Scientific Film Association are arranging three morning meetings for discussion: on Friday, October 8 and Monday, October 11, at the Royal Society of Medicine, and on Saturday, October 9, at SIMPL, 1-4 Lambeth High Street, S.E. Those wishing to send or bring medical or biological films for discussion should write to the Organizer Specialist Medical Sessions, International Scientific Film Congress, 34 Soho Square, London, W.1.

PUBLICATIONS

Psychiatric Examination: Extended History in Cases of Neurosis, by A. Spencer Paterson, M.D., M.R.C.P. (second edition H. K. Lewis & Co., Ltd., 9d.). These useful cards which give on one side questions for the establishment of provisional diagnosis, and on the other those for eliciting causal factors in cases of psychoneurosis, should be of great assistance to the practitioner when dealing with suspected psychoneuroses.

Sixty Years of Medical Defence, by Robert Forbes, M.B., Ch.B., J.P., gives the history of the Medical Defence Union from its inception in 1885 to its Jubilee in 1945. It is published by the Medical Defence Union, 49 Bedford Square, London, W.C.1.

OFFICIAL NOTICES

Surgeons Gowns and Coat Overalls.—Practitioners entering or returning to practice can obtain certificates for up to six gowns or coat overalls on application to the Ministry of Health, Whitehall, London, S.W.1; in Scotland to the Department of Health for Scotland, St. Andrew's House, Edinburgh; in Northern Ireland, to the British Medical Association House, Tavistock Square, London, W.C.1, enclosing stamped addressed envelope for reply.

Streptomycin Regulations, 1948, which came into force on August 1, 1948, bring streptomycin within the scope of the Penicillin Act, 1947.

Supplies of Diphtheria Anti-Toxin (E.C.L. 74) announces the arrangements made by the Minister of Health for supply free of charge of diphtheria antitoxin for use in an emergency by general practitioners.

The contents of the November issue which will include
section. eral Practice, will
the advertisement

minor operation, taking perhaps about five to ten minutes to perform. Such a single dose may be administered for, say, the setting of a fracture, the opening of an abscess, the passage of a cystoscope, or the manipulation of a joint. The difficulty here is to assess the dose with sufficient accuracy for the anæsthesia to last throughout the operation but not much longer. The intermittent method, described later, is the safer and more satisfactory way of giving thiopentone for even the shortest operation, but there are many occasions when a single dose is the practical way of meeting the situation. With slight modification, one of the earliest techniques described for pentothal and evipan still holds good.

When the surgeon is ready and the operation area draped, the patient is put to sleep as already described. Another pause of at least one-half to three-quarters of a minute is then made to allow the drug to circulate and the respiration, which has by now probably been depressed, to become well established again. As much thiopentone as has already been given is then injected very slowly, the needle withdrawn, and the operation immediately begun.

INTERMITTENT INJECTION

A better method and one more suitable when longer operations are proposed, is the repeated injection of moderate doses of thiopentone whenever the patient shows signs of coming round. The method is carried out in this manner:—

When the patient becomes unconscious a pause is made. An amount equal to about half the induction dose is then given and the operation starts. The needle is kept in the vein and whenever the patient reacts to the operation, say, by moving his arm or leg, wrinkling his eyebrows or perhaps by breathing deeply, a small additional dose is given. An interval of at least a half to one minute should be allowed between the injections, so that the effects of one may become apparent before the next is made. When a 5 per cent. solution is being used, each additional injection consists of about 1 c.cm. (i.e. 0.05 gm.). By this means operations lasting up to half-an-hour can be carried out.

The method is not very suitable for longer operations, unless the administrator is skilled. The difficulty of keeping the needle patent and in place over long periods of time makes other methods more suitable. In addition, when amounts of thiopentone in excess of 1 gm. are given they are followed by prolonged recovery and delay of return to consciousness, always a hazard and a definite disadvantage in circumstances when the patient must be ambulant in as short a time as possible. In general it is wiser not to choose intravenous anæsthesia when it is known that the operation is to last for longer than thirty minutes. If the operation is unexpectedly prolonged, a change should be made to an inhalation anæsthetic. By the time a patient has been anæsthetized with thiopentone for half-an-hour he is sufficiently depressed to make nitrous oxide and oxygen anæsthesia easy, even when the oxygen in the mixture is abundant. By this means the anæsthesia may be continued until the operation ends.

THE CONTINUOUS DRIP METHOD

Either the single dose injection or the intermittent method is likely to cater for the majority of the needs of the general practitioner. Those who wish

has shown that the great majority of patients are grateful for a thiopentone induction. There are exceptions, however. The following are examples of patients who not only do not care whether or not they have an injection, but in whom the use of thiopentone becomes an unwarranted hazard.

(1) *Infants and very young children*.—It is a matter for discussion whether the “mental trauma” of an injection carried out on a struggling baby is greater or less than a few breaths of ethyl chloride from an open mask. I have heard of a child’s arm being amputated as a result of intra-arterial injection of thiopentone in these circumstances. Extra-venous injection and subsequent ulceration are not uncommon.

(2) *The very old*.—I am of the opinion that the marked placidity of mind and fatalistic outlook so common at this extreme of life do not indicate an injection as a more acceptable alternative to a mask. Overdosage, not always successfully counteracted by subsequent resuscitation, is common in these patients, particularly when natural frailty is increased by disease.

(3) *Gravely ill patients* are in no mood to care how they are put to sleep. Neither the earthy-faced man dying of acute intestinal obstruction nor the wax-like girl dying of hæmorrhage from an ectopic pregnancy, care if a mask is put on to their face. Induction of anæsthesia in these patients with an inhalation anæsthetic is usually easy. If thiopentone must be used, the dose is likely to be strikingly small—perhaps a quarter or less of the dose which would be required by the same patient in good health. The circulation in these patients is slow too, and time must be allowed for the apparently minute dose to circulate from arm to brain. To give more or to be in a hurry is to risk overdosage, and in any case to depress respiration, making subsequent inhalation anæsthesia more difficult to administer.

It is impossible to advise a standard induction dose of thiopentone applicable to all patients. In the average patient who has already had, say, $\frac{1}{6}$ of a grain (11 mgm.) of morphine, 0.25 gm. of thiopentone is usually sufficient. The ill adult may need only 0.1 gm., or less. In the fit patient, 2 to 3 c.cm. of a 5 per cent. solution are injected, and this is followed by a pause of thirty seconds. The pause gives time for untoward events such as intra-arterial injection to become apparent and, in those with poor circulation, for the small initial dose to reach the brain and show its effect before more is administered. The injection is then continued very slowly until the patient loses consciousness. The injection should always stop as soon as the patient is asleep—the objective of the injection.

The time-honoured method of noting the onset of unconsciousness is to ask the patient to count. A less obtrusive practice is to engage the patient in light gossip. With experience, the patient need not be disturbed; his drooping eyelids give ample information to the watching anæsthetist that the injection may be stopped.

THIOPENTONE AS A SINGLE-DOSE ANÆSTHETIC

The second common use for thiopentone is as the sole anæsthetic for a

minor operation, taking perhaps about five to ten minutes to perform. Such a single dose may be administered for, say, the setting of a fracture, the opening of an abscess, the passage of a cystoscope, or the manipulation of a joint. The difficulty here is to assess the dose with sufficient accuracy for the anæsthesia to last throughout the operation but not much longer. The intermittent method, described later, is the safer and more satisfactory way of giving thiopentone for even the shortest operation, but there are many occasions when a single dose is the practical way of meeting the situation. With slight modification, one of the earliest techniques described for pentothal and evipan still holds good.

When the surgeon is ready and the operation area draped, the patient is put to sleep as already described. Another pause of at least one-half to three-quarters of a minute is then made to allow the drug to circulate and the respiration, which has by now probably been depressed, to become well established again. As much thiopentone as has already been given is then injected very slowly, the needle withdrawn, and the operation immediately begun.

INTERMITTENT INJECTION

A better method and one more suitable when longer operations are proposed, is the repeated injection of moderate doses of thiopentone whenever the patient shows signs of coming round. The method is carried out in this manner:—

When the patient becomes unconscious a pause is made. An amount equal to about half the induction dose is then given and the operation starts. The needle is kept in the vein and whenever the patient reacts to the operation, say, by moving his arm or leg, wrinkling his eyebrows or perhaps by breathing deeply, a small additional dose is given. An interval of at least a half to one minute should be allowed between the injections, so that the effects of one may become apparent before the next is made. When a 5 per cent. solution is being used, each additional injection consists of about 1 c.cm. (i.e. 0.05 gm.). By this means operations lasting up to half-an-hour can be carried out.

The method is not very suitable for longer operations, unless the administrator is skilled. The difficulty of keeping the needle patent and in place over long periods of time makes other methods more suitable. In addition, when amounts of thiopentone in excess of 1 gm. are given they are followed by prolonged recovery and delay of return to consciousness, always a hazard and a definite disadvantage in circumstances when the patient must be ambulant in as short a time as possible. In general it is wiser not to choose intravenous anæsthesia when it is known that the operation is to last for longer than thirty minutes. If the operation is unexpectedly prolonged, a change should be made to an inhalation anæsthetic. By the time a patient has been anæsthetized with thiopentone for half-an-hour he is sufficiently depressed to make nitrous oxide and oxygen anæsthesia easy, even when the oxygen in the mixture is abundant. By this means the anæsthesia may be continued until the operation ends.

THE CONTINUOUS DRIP METHOD

Either the single dose injection or the intermittent method is likely to cater for the majority of the needs of the general practitioner. Those who wish

for a smoother anæsthesia will sooner or later use the more elaborate technique of continuous drip infusion. The apparatus is similar to that used for intravenous saline, although for compactness air pressure supplied by a sigmoidoscope bellows may be used to drive the fluid into the vein, instead

of hanging the bottle on a stand and using gravity. If air pressure is to be used the patient must be safeguarded against the grave risk of air embolism. The use of an Oxford safety dripper (fig. 1), easily obtainable, will prevent this occurrence. The bottle is filled with a dilute solution of thiopentone (2 gm. dissolved in one pint of saline is a suitable dilution). The administrator must keep constantly in mind the dose which has already been administered. Thus, when the pint bottle is half empty the patient has already had 1 gm. of thiopentone. Weaker solutions may be used with an increased margin of safety, but a large bore needle becomes imperative or difficulty may be encountered in infusing the solution fast enough should the patient unexpectedly react.

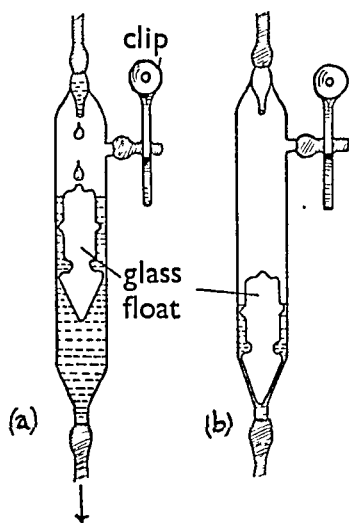


FIG. 1.—THE OXFORD SAFETY DRIPPER. As long as the liquid enters the drip feed chamber the glass float remains on the surface of the liquid (a). If air instead of liquid enters the chamber, the float falls on to its seating and prevents the passage of air (b).

SOME PRACTICAL DETAILS

There is little point in using thiopentone in stronger solution than 5 per cent., i.e. 0.5 gm. dissolved in 10 c.cm. of distilled water. There is, in fact, possibility of harm, for if injected outside the vein stronger solutions are likely to produce necrosis of the tissues, whilst even with the needle in its proper place thrombosis of the vein is frequent. Emphasis was formerly placed on the importance of using only solutions freshly made immediately before injection. Experience has shown that solutions may be used with safety so long as they are clear. In time, a precipitate appears due to deposition of thiopentone consequent on acidification of the solution by the atmosphere.

Syringes should be of all glass construction so that complete sterilization, either by dry heat or in an autoclave, is possible. The transmission of the virus of homologous serum jaundice is a serious risk attending the use of improperly sterilized syringes. The long incubation period of up to three or four months may give a false sense of security, for the connexion between the attack of jaundice and the intravenous injection is not overt.

The *needle* must be fine and sharp. Only so will an easy painless injection be made, and success assured with the smallest of veins. When intermittent injections are to be given the difficulty arises of keeping the needle in the vein and the syringe in the needle. Simple fixation of the syringe to the arm

by strapping or rubber band, allows blockage of the needle to take place due to seepage of blood into the needle tip. There are at least two efficient ways of preventing this blockage. The first is the inclusion of a simple tap between syringe and needle (fig. 2). Following each injection the tap is

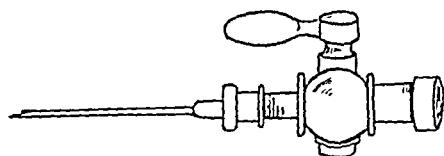


FIG. 2.—The tap is turned off between each injection to prevent blockage of the needle.

closed. Blood cannot now enter the needle. There is in addition no need to keep the syringe on the needle between injections. A more recent and most ingenious invention from Sweden is the "diaphragm needle" of Gordh (fig. 3), now easily obtainable in this country. The principle of this simple but effective device is appreciated by imagining the hub of an ordinary intravenous needle occluded by a small diaphragm of rubber. With the needle point placed in a vein, injections are made when desired through the diaphragm by another needle and syringe containing the thiopentone solution.

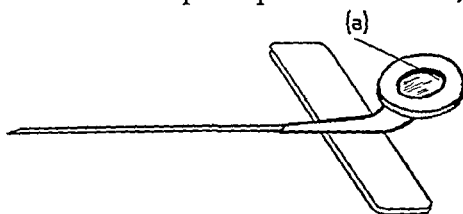


FIG. 3.—The diaphragm needle: (a) rubber diaphragm 1.5 mm. thick.

GENERAL PRECAUTIONS

As with any other general anæsthetic the patient should have had no food for at least two hours before the injection. If this preoperative period can be spent by the patient in relaxation and in acquiring tranquility, all the better. Once unconsciousness has occurred the anæsthetist must ensure that from that moment until consciousness returns his patient breathes easily and without obstruction, and that his colour remains a brilliant pink. If respiration is very shallow and quiet, a wisp of cotton-wool fixed to the tip of the patient's nose by a spot of petroleum jelly will indicate whether or not air is actually passing in and out of the lungs. If the patient is connected to an anæsthetic apparatus for the purpose of simultaneously receiving oxygen, or an inhalation anæsthetic, a more accurate guide to the depth of respiration and probable depth of anæsthesia is given by the movement of the breathing bag. Never for a moment should vigilance relax. If the anæsthetist's two hands are occupied with the injection, he must have a helper to support the patient's jaw and ensure a clear airway.

Although some anæsthetists regularly inject thiopentone into patients when sitting in the dental chair, the practice is not for the inexperienced. Thiopentone causes a temporary drop in blood pressure and susceptible individuals may give the anæsthetist some concern. Patients should be lying down.

If the patient is still unconscious when he leaves the immediate vicinity of the anæsthetist, clear instructions should be given to the nurse that he

must on no account be left alone until his pharyngeal reflexes have returned. Unattended patients, depressed after long intravenous anæsthesia, soon succumb when respiratory obstruction occurs. Many lives have been lost in the postoperative period through this cause. Morphine should not be given after intravenous anæsthesia, as indeed it should not after any other anæsthetic, unless the patient is either restless or in pain. Only so will dangerous depression due to a combined effect be avoided.

HAZARDS

The popularity of intravenous anæsthesia is maintained among patients who appreciate the comfort and pleasantness of going to sleep under the influence of thiopentone, and among anæsthetists who appreciate the simplicity of its administration. These virtues are well known: the risks which attend the use of intravenous anæsthesia are less well appreciated.

First and foremost is the danger of overdosage. It is particularly easy to give too large a dose to shocked or gravely ill people. In such patients a small dose of the order of 0.1 gm. produces an effect both of degree and duration similar to that produced by a dose several times greater in the healthy. The converse is also true: doses regarded as average for the robust may well be lethal to the same patient when exsanguinated or shocked. In these patients, if not in fact in all, pentothal should be injected slowly, a pause made after the first 2 to 3 c.cm., and the injection stopped altogether as soon as unconsciousness supervenes.

Equally serious, if not so overt at the time, is the injection of thiopentone into an artery. This accident was unheard of until the first reports appeared a few years ago. It is now known that many cases have occurred up and down the country, but as usual there has been an understandable though regrettable reluctance to publish them. As a result there are still many practitioners who use thiopentone but who do not appreciate the possibility or the gravity of this event. An aberrant ulnar artery lying just under the skin in the antecubital region is a not uncommon anatomical abnormality, and such a superficial artery is easily mistaken for a vein. This mistake is particularly liable to happen when an assistant manually compresses the upper arm with more vigour than discretion. The superficial artery, now no longer pulsating, looks and feels like a vein. The anæsthetist receives warning that his needle is in the artery by the intense, agonizing, and scalding pain in the forearm and hand which follows the injection. In many of the cases which have come to light, this unfortunate occurrence has led to gangrene and amputation of part of the limb, varying from finger-tip to forearm. Here then is another reason, and an important one, for pausing after the initial injection of a few c.cm. of thiopentone; the pause should be long enough to ensure, even in patients with very slow circulation, that the thiopentone, if injected into an artery, has reached the finger-tips before the patient is made unconscious. Any complaint of pain by the patient indicates withdrawal of the needle from the vessel.

No treatment, however ingenious or heroic, is known to prevent with certainty the dire results of intra-arterial injection. A harmless, possibly curative, and apparently effective treatment of the pain, is the immediate injection of a few c.cm. of 1 per cent. procaine into the same artery.

Subcutaneous injection of thiopentone, although of minor importance compared with intra-arterial injection, nevertheless causes pain, and may for the time being cause serious disability to the patient and worry to the anæsthetist. Cause and effect here are obvious, and litigation is a possibility which should be borne in mind. Injection into the tissues is followed at best by transient discomfort, and at worst by a painful, indolent and sloughing ulcer. The severity of the effect of extra-venous injection depends mainly upon the strength of the solution: 5 per cent., the common strength of thiopentone in use in this country, must not be exceeded. In America it is taught that $2\frac{1}{2}$ per cent. is the maximum permissible concentration. Aspiration of blood into the syringe before injection ensures that the needle is in the vein at the start and is a simple precaution that should never be neglected. A sharp eye on the skin overlying the point of the needle will detect the little bump which indicates that solution is being injected outside the vein. Confirmation is usually provided by a complaint of pain from the patient. If there is any doubt as to whether the needle is in the vein or not, it is better to stop the injection and try again. When venepuncture presents persistent difficulty it is better to use some other form of anæsthetic than to risk the possible complications which may follow a misplaced needle.

The traditional treatment for extra-venous injection is the application of moist heat. The latest suggestion is that the area should be infiltrated immediately with 1 per cent. procaine. Although this treatment is probably harmless, there are as yet no clinical reports of its effectiveness.

OVERDOSAGE

Of all the hazards of pentothal, that of overdosage remains the most serious. It shows itself by the cessation of respiration, soon followed, if not corrected, by arrest of the heart. This complication should not hold any terrors for the anæsthetist. The injection is stopped as soon as it is noticed that the patient has stopped breathing, and interest is concentrated from that moment on ensuring oxygenation until spontaneous breathing re-starts. In the majority of cases breathing starts within a few seconds without any active effort on the part of the anæsthetist, but if this period has passed, or if cyanosis makes its appearance, some form of artificial respiration should be started. This procedure should not be withheld because other people in the theatre might become alarmed. Everybody in contact with patients receiving intravenous anæsthesia should know that respiratory arrest is a possible and common complication and that artificial respiration is the surest way of rendering it innocuous.

A convenient method of *artificial respiration* for the anaesthetist is the rhythmical compression of the reservoir bag of an anaesthetic apparatus, filled with oxygen or air. While the bag is compressed, the mask is held firmly over the patient's face with

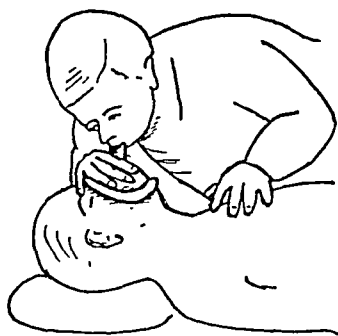


FIG. 4.—Direction inflation of the patient's lungs by blowing through an anaesthetic face-mask.

the expiratory valve closed. The mask is lifted between compressions to allow the lungs to empty into the air. Air or oxygen is thus repeatedly transferred from the bag to the patient's lungs, the chest rising and falling as this takes place. If such an apparatus is not readily to hand, the anaesthetist should without hesitation fall back on Elisha's method of artificial respiration, the effectiveness of which is so graphically described in the Bible (2 Kings, iv, 34). A note of elegance may be introduced by using an ordinary rubber anaesthetic mask. The mask is applied to the patient's face and a swab laid over the opening. The anaesthetist's lips are applied to the swab and by gently blowing through the opening of the mask, air from the anaesthetist's lungs, filtered from gross droplets by the gauze, is transferred to the patient. I can recommend this simple method of resuscitation most strongly, and can vouch for its effectiveness. By this means

alone lives will be saved which otherwise might be lost while time is spent in making available more complicated but not more effective means. So far as the better known methods of Schafer and Sylvester are concerned there is good experimental evidence that direct inflation of the lungs, obviously more convenient for an anaesthetist at the head of the patient, is by far the most effective of any method, in terms of the volume of respiratory exchange.

Artificial respiration and oxygenation of the patient come first. *Injection of resuscitative drugs* is secondary and can well be regarded as having little place in the treatment of overdosage during clinical intravenous anaesthesia. The two drugs most useful for this purpose are nikethamide and picROTOXIN. The former is suitable for the milder forms of overdose, perhaps when a rapid return to consciousness is desired rather than the restoration of efficient breathing after gross overdose. For the latter purpose picROTOXIN is the drug recommended. Nikethamide straight from the ampoule is slowly injected intravenously in doses of from 1 to 5 c.cm., depending upon the degree of depression. Within a few minutes the patient breathes deeply, moves about, perhaps opens his eyes, and even talks. PicROTOXIN is supplied as an 0.3 per cent. solution (i.e. 3 mgm. per c.cm.), 1 to 2 c.cm. of the solution of this potent drug being injected intravenously and thereafter repeated in doses of 0.5 c.cm. every minute until the patient shows signs of reflex activity, i.e. muscular twitchings, movements, or return to consciousness.

Bibliography

- Macintosh, R. R., and Mushin, W. W. (1946): *Brit. med. J.*, i, 908.
 —, and Pask, E. A. (1941): *Lancet*, ii, 10.
 Minnitt, R. J., and Gillies, John (1948): "Textbook of Anaesthesia," 7th edition, Edinburgh, chapter 18.

THE NEWER INHALATIONAL ANÆSTHETICS

By CARL S. HELLIJAS, M.D., AND RALPH M. TOVELL, M.L.

From the Department of Anesthesiology, Hartford Hospital, Connecticut, U.S.A.

CYCLOPROPANE

General characteristics.—The anæsthetic potency of cyclopropane is stated to be 100 per cent.; the period of induction is short, and respiratory arrest can be quickly attained. As the sole agent, it is most often satisfactory for surgical procedures requiring only moderate degrees of relaxation. In the more robust patient, however, profound relaxation can seldom be secured without the addition of other agents. In anæsthetic concentrations, cyclopropane has but little irritating effect on the respiratory tract; there is no initial stimulation of respiratory activity, of either central or reflex nature. Induction is therefore usually quiet. Respirations become progressively shallow during descent; the onset of respiratory paralysis occurs in the third plane. Premedication with sedative drugs enhances the depressing effect of cyclopropane and reduces the concentration necessary for respiratory arrest. The popular practice of inducing narcosis with pentothal sodium by the intravenous route adds its depressant effect to that of cyclopropane and renders induction with the latter agent slower. Pentothal sodium should be administered slowly and in sufficient amounts to induce light sleep only. The dosage of premedicating agents should be reduced when the use of cyclopropane is intended.

Mixtures of cyclopropane and oxygen can be highly explosive. Every known precaution must therefore be taken to prevent accidents.

Control of respiration.—Inadequate pulmonary ventilation increases the incidence of atelectasis and is ineffective in the removal of carbon dioxide from the alveoli. Augmentation of ventilation by gentle rhythmic pressure on the breathing bag permits greater use of the available alveolar bed and speeds the rate of removal of carbon dioxide. Inefficient respiratory exchange should not be permitted to continue unaided, and the anæsthetist may, when necessary, assume active control of respiration during the administration of cyclopropane. Lack of stimulation of respiratory activity, high content of oxygen in the respired atmosphere and removal of carbon dioxide by absorbents enable him to take control early in the period of maintenance. This method of control has been recommended during the performance of surgical procedures within the thorax. The abolition of respiratory movements facilitates surgical manœuvres at the pulmonary hilum and about the heart and great vessels. Relaxation of the abdominal musculature is often profound. This technique has also been employed to aid in the insertion of endotracheal catheters. The judicious use of curare, however, seems to have removed much of the need for "controlled respiration" for surgical

procedures within the abdomen or for intubation of the trachea. Ether may be added to the respired mixture while active respiration continues; the advantages of spinal and regional anæsthesia by appropriate methods further reduce the indications for a technique of questionable worth.

Side-effects.—A type of respiratory activity closely simulating that of an acute asthmatic attack infrequently occurs when cyclopropane is administered. The incidence is reported to be higher among those manifesting hypersensitivity to various allergens, among asthmatics and others suffering from respiratory diseases (Rovenstine and McKinnie Phelps, 1942). Stimulation of the vagus nerve by the parasympathomimetic action of cyclopropane has been suggested as the causative factor. Experimentally, cyclopropane produces bronchiolar constriction. This effect is enhanced by parasympathomimetic drugs and is blocked or prevented by atropine and similar drugs. Laryngospasm and cyanosis often accompany lower respiratory obstruction, and bronchiolar constriction may occur even in the presence of an endotracheal catheter and an abundant concentration of oxygen. The "rocking-boat" character of respiration, expiratory wheezing, and inability to inflate the lungs by manual pressure on the breathing bag usually make the diagnosis obvious. The intravenous administration of atropine or ephedrine, the addition of helium to the respired mixture, and the use of ether have been recommended as methods of therapy. The ready availability of ether and its known bronchodilator effect make it the agent of choice. In the absence of an endotracheal catheter, the increase of intrathoracic negative pressure developed by inspiratory efforts against a tightly closed glottis will in some instances promote the onset of pulmonary œdema. Prompt restoration of the patient's airway is of prime importance in the prevention of untoward sequelæ. Introduction of an endotracheal catheter or severe surgical stimulation under incomplete anæsthesia may initiate the syndrome of lower respiratory obstruction (Nosworthy, 1948). The suggested treatment in this case is descent to a deeper plane of anæsthesia before undertaking such procedures.

Recent observations suggest that *curare* reduces the severity of troublesome reflex phenomena associated with traction on viscera (Hewer, 1946). This may be due to delay or block of impulses between preganglionic and postganglionic fibres within the autonomic pathways (Langley, 1918). The combination of cyclopropane and *curare* produces relaxation equal to that of spinal anæsthesia, and unless the plane of general anæsthesia is too light, there is seldom significant evidence of reflex reaction to manipulation of abdominal viscera.

THE EFFECT OF CYCLOPROPANE ON THE HEART

The chief interest in the pharmacology of cyclopropane has focused upon the effects of the drug on the heart. During cyclopropane anæsthesia there is significant dilatation of the heart, with a decrease in the efficiency of systole (Brace *et al.*, 1941). There may be direct toxic effects on the cardiac

musculature. The similarity of changes induced in the electrocardiogram by cyclopropane to those caused by anoxia formed the basis for an earlier explanation of these effects (Robbins, 1940). Disturbances of conduction, however, occur in the presence of a high arterial content of oxygen (Orth *et al.*, 1939). Other observations involved the parasympathomimetic properties of cyclopropane (Adriani and Rovenstine, 1942). Sensitization of the cardiac conducting mechanism was regarded as the effect of increased vagal tone: those drugs which stimulate the vagus nerve enhanced the effects of cyclopropane; parasympatholytic agents abolished or decreased the severity of these disturbances. The increase of vagal tone induced by morphine promoted the onset of bradycardia and cardiac irregularities; the barbiturates reduced vagal tonus and inhibited the production of arrhythmias (Robbins *et al.*, 1939). More recent work has demonstrated the relative lack of effect of either morphine (Allen *et al.*, 1945) or barbiturates (Orth, Wangeman and Meek, 1941) on the occurrence of irregularities during cyclopropane anæsthesia. Another theory implicated an "arrhythmia centre" in the hypothalamus (Thienes, Greeley and Guedel, 1941). This area remained active following depression of the respiratory centre and promoted the onset of disturbances of cardiac rate and rhythm. Descent into deeper anæsthesia by means of controlled respiration depressed this centre, with subsequent restoration of normal rate and rhythm. The existence of the centre is in doubt (Lee *et al.*, 1943). Electrocardiographic tracings have frequently shown that the regular heart beat in deep cyclopropane anæsthesia is an auriculo-ventricular nodal rhythm. The serious import attributed to nodal rhythm by cardiologists justifies abandonment of the production of deep anæsthesia with cyclopropane alone.

Methods of control.—Investigation of the arrhythmias induced by epinephrine during cyclopropane anæsthesia has cast new light on the problem. Cyclopropane increases the irritability of the cardiac conducting mechanism. Epinephrine acts on the sensitized tissue by direct effect on the cardiac myoneural junctions. Doses too small to produce an effect in the unanæsthetized animal will cause arrhythmias in the animal sensitized by cyclopropane: these irregularities are often ventricular tachycardia and ventricular fibrillation. Animal experiments have shown that both epinephrine and cyclopropane must reach the heart; in addition, a centre above the pons as well as the cardiac sympathetic pathways must be intact (Allen, Stutzman and Meek, 1940). Lesions of the brain stem, decerebration, or extensive bilateral thoracic sympathectomy abolish the effect of epinephrine on the sensitized heart. Vagotomy has little effect on the production of arrhythmias (Allen *et al.*, 1945). Recent work indicates that impulses from the mesentery transmitted through the cœliac plexus to the spinal cord and thence to a centre in the brain are involved in sensitization of the heart (Stutzman *et al.*, 1947). Bilateral lumbodorsal sympathectomy and splanchnicotomy prevent the action of epinephrine. It is evident that the sympathetic pathways are chiefly involved in the action of cyclopropane on cardiac rate and

rhythm; the parasympathetic system apparently exerts only a minor effect.

Marked bradycardia or tachycardia should be regarded as harmful. Decreasing the concentrations of cyclopropane and increasing the proportion of oxygen will usually restore the normal status. Ether may be added to the respired mixture to provide both greater relaxation and protection from the effects of cyclopropane. The administration of curare will often promote satisfactory surgical conditions with a level of anæsthesia above that likely to produce arrhythmias. In no circumstances should the use of epinephrine be permitted during the administration of cyclopropane. Other common vasoconstrictors have been employed in moderate dosage without evidence of harm (e.g. cobefrin, ephedrine). Pituitrin should be avoided (Belinkoff, 1944). Constriction of the coronary arteries induced by pituitrin added to the toxic effects of cyclopropane may produce sudden cardiovascular collapse.

Early experiments showed that procaine gives some protection from arrhythmias provoked by cyclopropane and epinephrine (Allen *et al.*, 1941). Procaine reduces the irritability of the myocardium, demonstrated both by topical application to the heart and by intravascular injection (Mautz, 1936). War-time experiences afforded dramatic evidence of the value of procaine in the presence of acute cardiac dysfunction (Burstein, 1946). Rapid intravenous injection of a 1 per cent. solution of procaine restored normal cardiac rhythm in the cases reported. Similar experiences in later civilian practice are confirmatory (Dritz, 1948; Cross, 1948). Procaine in solution may be injected rapidly in moderate doses without ill-effect during general anæsthesia; caution must be exercised in its administration to the un-anæsthetized subject. The use of procaine in more concentrated solutions in such emergencies prompted the employment of dilute solutions throughout surgical procedures when cardiac arrhythmias existed before operation or were likely to occur at some point during the operation (Tovell and Barbour, 1948). Such instances include major intrathoracic and combined abdomino-thoracic procedures. The concentration of procaine is usually 0.2 per cent. Beneficial results have been observed, with improvement in the quality of the pulse, steadying of the rate and rhythm, and avoidance of harmful reflex sequelæ which commonly follow traction on thoracic and abdominal viscera.

INDICATIONS FOR CYCLOPROPANE INDUCTION

Cyclopropane may be employed with caution for induction in some instances in which arrhythmias and other evidence of *cardiac disease* exist before operation. Early addition of ether to the respired mixture promotes stabilization of cardiac action and increases muscular relaxation without resort to deeper levels of anæsthesia. The comparative lack of excitement during induction and the high content of oxygen in the anæsthetic mixture bespeak a smoother course of anæsthesia for the patient suffering from congenital heart disease. The value of cyclopropane in the presence of *shock* from severe loss of blood has been demonstrated (Hershey and Rovenstine, 1944).

A recent report indicates the possibility of major decreases in blood pressure following prolonged anæsthesia in which cyclopropane alone has been administered by the closed system (Dripps, 1947). Hypotension in this instance may be due partly to the rapid removal of carbon dioxide, the retention of which has been fostered during anæsthesia by the depressant action of cyclopropane on respiration.

Children.—The value of cyclopropane in anæsthesia for the infant is limited. The increase in dead space, greater resistance with the closed system, and depression of respiration sharply limit its applications. The semi-open system of administration to infants is costly and usually productive of an uneven course of anæsthesia. The to-and-fro closed system may be employed for older children with some success. The open or semi-closed administration of diethyl ether, however, remains the technique of choice for infants and children. The closed endotracheal system of cyclopropane anæsthesia was initially employed in surgical intervention on the great blood vessels in children suffering from congenital heart disease. Continued experience in anæsthesia for this form of operation indicates that ether is here also unsurpassed.

TRICHLORETHYLENE

The application of trichlorethylene to clinical anæsthesia followed the observation of its effects on workers employing the impure product for industrial purposes (Hewer, 1941, 1943). Pure preparations were tested in the treatment of trigeminal neuralgia; the effect on function of this nerve was considered to be specific. Later evaluation indicated that the relief produced is based on the marked analgesic properties of the drug.

Method of administration.—Trichlorethylene is an anæsthetic agent of moderate potency. It produces muscular relaxation of variable degree, usually insufficient for major procedures within the abdomen. The maximum relaxation obtained with this drug appears early in the third stage. Further saturation in attempt to increase the degree of relaxation is unwarranted. The tendency to untoward reactions is proportional to the level of saturation. The inferior volatility of the agent prevents large increases in concentration. The vapour pressure is low under standard conditions. At room temperature (20°C.), the maximum saturation is from 6 to 7 volumes per cent. (Macintosh and Mushin, 1947). The open-mask method of inhalation is therefore unsuitable. Cooling of the mask by evaporation of the liquid and removal of vapour by respiration further reduce the available concentration. To secure adequate concentrations, trichlorethylene should be administered by the semi-closed technique: devices utilizing wicks or streams of gases over or through the liquid are satisfactory. The basal flow of gases in the closed system will not produce sufficient evaporation. In addition, the closed system has been discarded because of toxic reactions.

Induction is usually rapid and smooth. There is little irritation of the respiratory passages. Pentothal sodium may be employed in small doses

without seriously hampering further induction with trichlorethylene. The combination of nitrous oxide and oxygen is the more popular vehicle for volatilization. The concentration of trichlorethylene can be increased relatively rapidly, allowing early descent to the upper planes of the third stage. Very small increments of the drug are needed thereafter for maintenance (Hewer, 1941, 1946; Haworth and Duff, 1943). Increased saturation is difficult to attain. Deep anæsthesia should be avoided, as recovery may be delayed (Durrans, 1943), and disturbances of respiration and circulation are more likely to occur. Other agents and methods should be called upon to provide a greater depth of anæsthesia or relaxation.

The *effect of trichlorethylene on respiratory activity* constitutes a major guide in its administration. During the first stage, breathing is unchanged in rate, rhythm and amplitude. Some excitement with varying changes in respiratory rhythm occurs not infrequently in the second stage. In the first plane of the third stage, breathing is quiet, automatic and sometimes shallow. The amplitude of inhalation and exhalation are nearly equal. A small increase in rate usually takes place at this point. Tachypnœa may appear gradually or suddenly; respiratory arrest is then likely to occur unless the concentration of trichlorethylene is diminished or inhalation halted. Tachypnœa occurs more frequently when the concentration is increased too rapidly or when greater saturation is attempted. Cyanosis and convulsions may appear (Goldschmidt, 1943; Garland, 1942). A recent experimental analysis points to possible causes for the changes in respiratory activity (Whitteridge and Bülbring, 1946). Sensitization of the pulmonary stretch-receptors produces an increase in rate and a decrease in depth of respiration, with a decrease in pulmonary volume at the end of inhalation. Stimulation of the deflation-reflex further augments the rate of respiration and increases the amount of air retained in the lungs at the end of exhalation. Trichlorethylene stimulates these reflexes throughout the period of exposure; finally, failure of stimulation occurs suddenly, followed by respiratory arrest. Vagotomy abolishes these effects. Disturbances of respiratory activity can be minimized by maintenance in upper planes of the third stage and by avoiding sudden increases in concentration. The addition of diethyl ether to the respired mixture often restores normal rate and rhythm when abnormalities are present.

Cardiovascular effects.—Variations in cardiac rate and rhythm depend largely upon the concentration employed. In lighter planes, sinus bradycardia and occasional premature contractions are commonly observed. In deeper planes, more significant alterations often occur: auriculo-ventricular block; auriculo-ventricular nodal rhythm; displacement of the pacemaker, with ectopic foci initiating premature contractions in both auricles and ventricles; pulsus bigeminus; multiple focus ventricular tachycardia (Waters, Orth and Gillespie, 1943; Barnes and Ives, 1944). Trichlorethylene may sensitize the heart to the action of epinephrine (Waters, Orth and Gillespie, 1943; Gordon and Shackleton, 1943), and hæmostasis with this vasocon-

strictor should not be permitted. Maintenance in a light plane and the avoidance of anoxia minimize the incidence of cardiac irregularities. When such variations are present, the treatment includes decreasing the concentration of trichlorethylene, increasing the proportion of oxygen, and adding diethyl ether to the mixture.

There is little change in blood pressure in the absence of marked loss of blood or severe surgical trauma. Oozing from capillaries is minimal (Brittain, 1948; Hewer, 1943). Cardiovascular changes were reported with a trichlorethylene-ether sequence in closed system (Johnson, 1944). The more frequent complications were: an increase in blood pressure and pulse pressure, epistaxis, bleeding from the gums and hæmorrhage from the site of operation (e.g. hæmorrhoidectomy). Admitting air to the system and changing to an open technique with ether arrested or prevented further occurrences of similar nature.

Other side-effects.—Recovery from trichlorethylene is as a rule rapid and uneventful. Instances of delayed recovery have usually followed prolonged surgical procedures or maintenance in deeper planes. There is little nausea or vomiting. Convulsions may occur during maintenance or recovery, subsequent for the most part to increased saturation and often associated with respiratory arrest. Urticarial rashes occasionally appear. Pulmonary complications are reported to be fewer and less severe than those following the use of ether. Trichlorethylene has been employed during surgical procedures for tuberculosis and other pulmonary diseases without apparent aggravation of the underlying condition. Its use in the presence of cardiovascular disease should be guarded. The effect on renal function is minimal. Hepatic function may be transiently impaired (Armstrong, 1947), and acute yellow atrophy has been observed (Herdmann, 1945; Wyant, 1945). The administration of trichlorethylene to patients suffering from hepatic dysfunction is inadvisable.

The inhalation of this agent by the closed system has been abandoned. The occurrence of *cranial nerve palsies* stimulated investigation of the possible reaction of trichlorethylene with soda-lime.

It had been noted that soda-lime exposed to this drug had a sour smell and generated temperatures higher than the average. *Trichlorethylene decomposes* in the presence of alkali, with production of significant amounts of dichloroacetylene and dichloroacetylchloride (McClelland, 1944; Firth and Stuckey, 1945). This reaction is enhanced by heat and by lack of moisture. The presence of ether or moisture retards decomposition. The products of degradation may be oxidized to form phosgene and hydrochloric acid; an excess of trichlorethylene retards oxidation. Dichloroacetylene is explosive in air; phosgene and hydrochloric acid are intensely irritating to the respiratory tract. The contamination of soda-lime by trichlorethylene may give rise to complications when the same machine is used again in closed system with other agents. Emptying the canister before the use of trichlorethylene will prevent untoward reactions from the anæsthetic at hand. The machine should be thoroughly flushed before inserting soda-lime for subsequent procedures.

Trichlorethylene is not explosive in the concentrations obtainable during anæsthesia or under conditions prevailing in the average operating room (Jones and Scott, 1943). Phosgene and chlorine were detected under experimental conditions simulating the use of trichlorethylene in the presence of cautery (Hewsppear, 1944).

A high basal flow of gases and intermittent application of the cautery for short periods prevented the generation of significant amounts of either contaminant. In clinical practice, the flow of gases should be at least five litres per minute. The concentration of products of decomposition will then be less than that likely to cause untoward reactions.

Trichlorethylene is therefore suitable for procedures of short duration and those requiring only moderate relaxation in which the semi-closed system will provide optimal conditions. Diethyl ether, curare, spinal and regional anaesthesia may be employed as adjuvants to secure greater relaxation and depth of anaesthesia. Trichlorethylene alone produces sufficient relaxation of the jaw to permit the introduction of endotracheal catheters. The endotracheal administration of this agent is satisfactory for neurosurgical procedures (Brittain, 1948; Ayre, 1944). The marked degree of analgesia of the first stage is particularly suited to minor procedures, e.g. manipulation of fractures, dental extractions. Appropriate devices permit the auto-administration of trichlorethylene and air for dental work, relief of the pains of labour, and other minor purposes (Barratt and Platts, 1946; Hyatt *et al.*, 1947). Amnesia is observed in a significant number of obstetrical patients.

DIVINYL ETHER

Divinyl ether is now employed only for induction and for anaesthesia of very short duration. It is four times more potent than diethyl ether but its margin of safety is comparatively low (Stewart, 1941; Draper and Whitehead, 1940, 1942). Maintenance with divinyl ether is as a rule erratic. The low boiling point, 28.3°C ., renders the establishment of smooth anaesthesia difficult, particularly in higher environmental temperatures. Muscular relaxation is variable and often inadequate.

Method of administration.—The open method of administration is preferred. Induction is rapid, and the period of excitement is short-lived. Muscular rigidity and copious salivation are often observed in the second stage, but upon entry into the third stage the respirations become quieter and more regular. The respiratory rate is often increased, and the respiratory excursions are sometimes rapid and shallow. Stertor is occasionally marked. If the concentration is increased too rapidly cyanosis will appear. Overdosage is easily accomplished. Attention to the rate of administration, to the ingress of air beneath the mask and to the patency of the airway is essential. Oxygen should be administered when evidence of toxicity, debilitation or anaemia is present. Muscular movements may persist during maintenance (Livingstone *et al.*, 1940). Similar activity has been observed in the experimental animal (Orth, *et al.*, 1940): "running movements" continued in most instances until respiratory paralysis was complete. Transsection of the spinal cord did not abolish them; apparently the site of stimulus lay within the cord. Irritation of the central nervous system was suggested as a cause of the muscular activity (Martin and Rovenstine, 1941). Ocular motion may also be evident in the deeper planes of anaes-

thetia. The accepted signs of anæsthesia are therefore unreliable. Divinyl ether is eliminated rapidly in the early postoperative period. Recovery is prompt; but nausea and vomiting often occur.

The sequence of divinyl ether—diethyl ether is a popular anæsthetic for *infants and children*. When light sleep has been obtained with divinyl ether, the induction is completed with diethyl ether. The rate of administration of diethyl ether should be sufficiently rapid to permit adequate saturation with this agent while recovery from divinyl ether takes place. Mixtures of divinyl ether and diethyl ether are not satisfactory. The differences in volatility and rate of effect make it difficult to estimate the degree of saturation with either agent. Convulsions may appear at any time during the administration of divinyl ether or during recovery (Martin and Rovenstine, 1941; Dawkins, 1940). In the divinyl ether—diethyl ether sequence, convulsions may occur shortly after the change to diethyl ether. A cautious induction with divinyl ether accompanied by adequate concentrations of oxygen will largely obviate the appearance of convulsions. Preliminary basal narcosis with pentothal sodium per rectum gives promise of reducing the incidence and severity of convulsive activity.

Contraindications.—Hepatic dysfunction or disease contraindicates the use of divinyl ether. Evidence of injury to the liver has been observed both clinically and experimentally (Hawk, *et al.*, 1941). The administration of divinyl ether for long periods or on repeated occasions to the same patient is therefore inadvisable. Impairment of renal function is similar in degree to that produced by diethyl ether. There is no evidence of sensitization of the heart to epinephrine or other commonly used vasoconstrictors (Orth, *et al.*, 1940). Sino-auricular acceleration of the heart occurs frequently. The blood pressure is well maintained in the lighter planes of anæsthesia.

Divinyl ether decomposes in the presence of light, heat, oxygen and acids: alkalis retard the rate of deterioration. The drug is stabilized by the addition of absolute alcohol and phenyl-alpha-naphthylamine (vinethene—Merck). In practice, the vinethene remaining in a bottle that has been opened and recapped is usually discarded after seven to ten days. Experimental evidence indicates that the product is suitable for use for much longer periods (Adriani, 1941).

EXPERIMENTAL AGENTS

The search for new anæsthetic agents has produced several experimental compounds. A few appear to deserve further clinical evaluation.

N-propyl methyl ether (metopryl) is similar to diethyl ether in its effects on the organism (White, *et al.*, 1946; Fisher and Whitacre, 1947; Rochberg, 1947). It is 25 per cent. more potent than ether, but there is little irritation or stimulation of the respiratory tract in anæsthetic concentrations. Cardiac rate and rhythm and blood pressure are unaltered in lighter planes of anæsthesia. There is no evidence of injury to the liver. The effects on renal function are similar to those produced by diethyl ether. The pharyngeal

and laryngeal reflexes are promptly depressed. Muscular relaxation may be inadequate. Induction is as a rule shorter than when diethyl ether is employed. Maintenance is smoother when adjuvant agents (nitrous oxide, cyclopropane or diethyl ether) are also administered. Recovery is comparatively prompt. Nausea and vomiting are common during this period. Metopryl may be administered by the open, semi-closed or closed system.

Isopropenyl vinyl ether (propethylene ether) is an isomer of cyclopropyl vinyl ether (cyprethylene ether) (Davis and Krantz, 1944). Its potency is three to four times that of diethyl ether. Its low volatility renders the use of a large evaporating surface necessary. The period of induction is short; small doses are required for a given length of anæsthesia. The muscular relaxation is comparable to that produced by diethyl ether. There is mild stimulation of respiration, and respiratory movements are full and regular. Cardiac rate and rhythm are well maintained, and the blood pressure is unaffected by average anæsthetic concentrations. No untoward effects on the liver or kidneys have been noted. Adequate anæsthesia can be produced with either of the common methods of administration. Supplemental agents may be employed as desired.

N-propyl ethyl ether is from one and one-half to two times more potent than diethyl ether. The effects on the organism are similar (Brown and Lucas, 1940; Griffith and MacLeod, 1947). There may be greater depression of respiration in deeper planes of anæsthesia than with ether. The blood pressure is well maintained. Any of the accepted methods may be used in the administration of *n*-propyl ethyl ether. Adjuvant agents contribute to the smoothness of induction and maintenance. Induction and recovery are similar to those observed with ether. Apparently there is no contraindication to the use of epinephrine. The relative lack of bleeding at operation has been noted.

These three experimental ethers have not received wide clinical acceptance. The results of future experimentation must be awaited before their places in the armamentarium of anæsthetists can be definitely established.

References

Cyclopropane

- Adriani, J., and Rovenstine, E. A. (1942): *Anesth. Analg.*, **21**, 111.
- Allen, C. R., et al. (1945): *Anesthesiology*, **6**, 261.
- , Stutzman, J. W., and Meek, W. J. (1940): *Ibid.*, **1**, 158.
- , —, Slocum, H. C., and Orth, O. S. (1941): *Ibid.*, **2**, 503.
- Belinkoff, Stanton (1944): *Amer. J. Obst. Gynec.*, **48**, 109.
- Brace, D. E., Scherf, D., and Spire, L. J. (1941): *Anesthesiology*, **2**, 261.
- Burstein, Charles (1946): *Ibid.*, **7**, 113.
- Cross, Robert R. (1948): In the press.
- Dripps, Robert D. (1947): *Anesthesiology*, **8**, 15.
- Dritz, Harvey F. (1948): In the press.
- Hershey, S. G., and Rovenstine, E. A. (1944): *Anesthesiology*, **5**, 149.
- Hewer, C. Langton (1946): *Brit. med. Bull.*, **4**, 110.
- Langley, J. N. (1918): *J. Physiol.*, **52**, 247.

- Lee, W. Vernon, *et al.* (1943): *Anesthesiology*, 4, 487.
 Mautz, F. R. (1936): *J. thorac. Surg.*, 5, 612.
 Nosworthy, Michael D. (1948): *Anæsthesia*, 3, 86.
 Orth, O. S., *et al.* (1939): *J. Pharmacol. exp. Therap.*, 67, 1.
 —, Wangeman, C. P., and Meek, W. J. (1941): *Anesthesiology*, 2, 628.
 Robbins, B. H. (1940): "Cyclopropane Anesthesia," Baltimore.
 —, Baxter, J. H., and Fitzhugh, O. G. (1939): *Ann. Surg.*, 110, 84.
 Rovenstine, E. A., and Phelps, McKinnie L. (1942): *J. thorac. Surg.*, 11, 565.
 Stutzman, J. W., *et al.* (1947): *Anesthesiology*, 8, 579.
 Thienes, C. H., Greeley, Paul O., and Guedel, A. E. (1941): *Ibid.*, 2, 611.
 Tovell, Ralph M., and Barbour, Charles M., Jun. (1948): In the press.

Trichlorethylene

- Armstrong, D. M. (1947): *Anæsthesia*, 2, 45.
 Ayre, Philip (1944): *Brit. J. Anæsth.*, 19, 17.
 Barnes, C. G., and Ives, John (1944): *Proc. Roy. Soc. Med.*, 37, 528.
 Barratt, A., and Platts, S. H. B. (1946): *Brit. med. J.*, ii, 10.
 Brittain, G. J. C. (1948): *Anæsth. Analg.*, 27, 145.
 Durrans, S. F. (1943): *Lancet*, ii, 191.
 Firth, J. B., and Stuckey, R. E. (1945): *Ibid.*, i, 814.
 Garland, Ysobel (1942): *Brit. med. J.*, ii, 607.
 Goldschmidt, Margot W. (1943): *Lancet*, ii, 414.
 Gordon, Roderick A., and Shackleton, R. P. W. (1943): *Brit. med. J.*, i, 380.
 Haworth, James, and Duff, Alexander (1943): *Ibid.*, i, 381.
 Herdmann, K. N. (1945): *Ibid.*, ii, 689.
 Hewer, C. Langton (1941): *Brit. med. J.*, i, 924.
 — (1943): "Recent Advances in Anæsthesia and Analgesia (Including Oxygen Therapy)," 4th edition, London and Philadelphia, p.106.
 — (1943): *Proc. Roy. Soc. Med.*, 36, 463.
 — (1946): *Brit. med. Bull.*, 4, 108.
 Hewspear, David (1944): *Brit. J. Anæsth.*, 19, 81.
 Hyatt, A. L., Gardener, T. H., and Elam, J. (1947): *Brit. med. J.*, ii, 27.
 Johnson, Emily E. (1944): *Brit. J. Anæsth.*, 19, 71.
 Jones, G. W., and Scott, G. S. (1943): *Anesthesiology*, 4, 441.
 McClelland, Margaret (1944): *Proc. Roy. Soc. Med.*, 37, 526.
 Macintosh, R. R., and Mushin, William W. (1947): "Physics for the Anæsthetist," Oxford, and Springfield, Illinois.
 Waters, R. M., Orth, O. S., and Gillespie, N. A. (1943): *Anesthesiology*, 4, 1.
 Whitteridge, D., and Bülbring, E. (1946): *Brit. med. Bull.*, 4, 85.
 Wyant, G. M. (1945): *Brit. med. J.*, ii, 820.

Divinyl Ether

- Adriani, John (1941): *Anesthesiology*, 2, 191.
 Dawkins, C. J. M. (1940): *Brit. med. J.*, i, 163.
 Draper, W. B., and Whitehead, R. W. (1940): *Anæsth. Analg.*, 19, 76.
 — (1942): *Lancet*, i, 442.
 Hawk, M. H., Orth, O. S., and Pohle, F. J. (1941): *Anesthesiology*, 2, 388.
 Livingstone, Huberta M., *et al.* (1940): *J. Amer. med. Ass.*, 115, 1353.
 Martin, Stevens J., and Rovenstine, E. A. (1941): *Anesthesiology*, 2, 285.
 Orth, O. S., *et al.* (1940): *Ibid.*, 1, 246.
 Stewart, H. Boyd (1941): *Ibid.*, 2, 635.

Experimental Agents

- Brown, W. E., and Lucas, G. H. W. (1940): *Canad. med. Ass. J.*, 43, 526.
 Davis, E. Hollister, and Krantz, John C., Jun. (1944): *Anesthesiology*, 5, 159.
 Fisher, A. J., and Whitacre, R. J. (1947): *Ibid.*, 8, 156.
 Griffith, Harold R., and MacLeod, Enid J. (1947): *Ibid.*, 8, 615.
 Rochberg, Samuel (1947): *Ibid.*, 8, 637.
 White, M. T. L., Shane, S. M., and Krantz, J. C., Jun. (1946): *Ibid.*, 7, 663.

ANÆSTHESIA IN MINOR SURGERY

By T. McW. MILLAR, M.B., F.R.C.S.ED.

Assistant Surgeon, Royal Infirmary, Edinburgh.

SURGERY and anæsthesia have both become such highly specialized branches of medicine that, as time goes on, the number of general practitioners who practise major surgery must steadily decline; a process which will undoubtedly be hastened by the advent of the National Health Service. When faced with even a minor surgical problem, many practitioners with little bent or liking for the practice of surgery will usually endeavour to obtain the assistance of a surgical colleague, and for those who practise within easy reach of a surgical hospital such assistance will normally be readily obtained. But those with surgical leanings and those who do not have ready access to surgical assistance will continue to carry out minor surgical procedures. The performance of even minor surgical operations in the patient's own home is never a very satisfactory procedure, but it may be hoped that in the future, as health centres, cottage hospitals and the like are developed, better facilities for surgical work may become available to most practitioners.

Good anæsthesia is of course as desirable for minor as for major operations. Anæsthesia should be as good as possible, and it should leave the patient with a minimum of unpleasant memories and sequelæ. The psychological trauma inflicted on many patients in the process of being anæsthetized, often for minor operations, is often revealed when the patient has later to undergo another operation: the anæsthetic is feared more than the operation.

Choice of anæsthetic.—These preliminary remarks lead to the questions: What type of anæsthetic may be used for minor surgery? What points should influence the practitioner in choosing the type of anæsthetic to be used? The practitioner may have little choice because he is working alone, and it may be impossible or highly inconvenient for him to obtain the assistance of a colleague to anæsthetize the patient. He must then adopt one of three alternatives:—(1) He may do the operation without an anæsthetic: a course of action justified and possible only in a limited group of cases, for example, suture of simple wounds, incision of acute abscesses. (2) He may administer a general or an intravenous anæsthetic himself and then perform the operation; again a line of action justifiable only in emergency cases. Unless he has the assistance of a trained nurse to look after the unconscious patient, his attention will inevitably be divided between the anæsthetic and the operation. (3) He may use local analgesia: a method which has the great advantage that it can be carried out efficiently single-handed.

GENERAL ANÆSTHESIA

Assuming that assistance is available in the shape of an anæsthetist, what are the *pros* and *cons* for using a general anæsthetic for a minor operation? The patient must first be considered, because:—

(1) He or she may prefer this form of anæsthesia.

(2) The patient may be temperamentally unsuited for operation under local analgesia, although this difficulty may be overcome by suitable premedication.

(3) As a rule children should have a general anæsthetic.

(4) Medical reasons may make the administration of a general anæsthetic inadvisable, although this will seldom be the case if the intervention is a minor one and the services of a skilled anæsthetist are available.

On the other hand, the practitioner may not like to operate on a conscious patient—a dislike that may be largely due to unfamiliarity with the technique of local analgesia or to lack of the skill and gentleness which are necessary when this method is used. When a skilled anæsthetist is available, the surgeon will be well advised to decide the type of anæsthetic to be used in consultation with the anæsthetist, or to leave the matter entirely to him. If a general practitioner is to administer the anæsthetic he must, of course, use the method with which he is most familiar.

Although a well-given general anæsthetic is completely adequate for any minor operation, it has its disadvantages:—(1) Unpleasant after-effects, such as vomiting, which is particularly undesirable if the patient has recently had a heavy meal; (2) the time required for the patient to recover, a period during which he should be under observation and for which accommodation must be provided—an awkward period if the practitioner has operated in his own surgery, or is pressed for time; (3) the ever-present element of danger in giving a general anæsthetic—a danger which is not related to the extent of the operation, but directly to the administration of the anæsthetic.

INTRAVENOUS ANÆSTHESIA

These observations apply to general anæsthesia by inhalational methods, but reference must also be made to the use of intravenous anæsthetics, particularly thiopentone sodium (pentothal), in the practice of minor surgery. As the whole subject of intravenous anæsthesia is dealt with in another article in this symposium, only a brief reference need be made here.

From both the surgeon's and the patient's point of view intravenous anæsthesia is excellent for minor surgery. The simple apparatus required, the rapid induction, the satisfactory depth and duration of anæsthesia, the rapidity of recovery of consciousness after a small dose and the lack of after-effects—these constitute an impressive list of advantages of the method. On the other hand, the dangers must not be forgotten—dangers associated

ANÆSTHESIA IN MINOR SURGERY

By T. McW. MILLAR, M.B., F.R.C.S.Ed.

Assistant Surgeon, Royal Infirmary, Edinburgh.

SURGERY and anæsthesia have both become such highly specialized branches of medicine that, as time goes on, the number of general practitioners who practise major surgery must steadily decline; a process which will undoubtedly be hastened by the advent of the National Health Service. When faced with even a minor surgical problem, many practitioners with little bent or liking for the practice of surgery will usually endeavour to obtain the assistance of a surgical colleague, and for those who practise within easy reach of a surgical hospital such assistance will normally be readily obtained. But those with surgical leanings and those who do not have ready access to surgical assistance will continue to carry out minor surgical procedures. The performance of even minor surgical operations in the patient's own home is never a very satisfactory procedure, but it may be hoped that in the future, as health centres, cottage hospitals and the like are developed, better facilities for surgical work may become available to most practitioners.

Good anæsthesia is of course as desirable for minor as for major operations. Anæsthesia should be as good as possible, and it should leave the patient with a minimum of unpleasant memories and sequelæ. The psychological trauma inflicted on many patients in the process of being anæsthetized, often for minor operations, is often revealed when the patient has later to undergo another operation: the anæsthetic is feared more than the operation.

Choice of anæsthetic.—These preliminary remarks lead to the questions: What type of anæsthetic may be used for minor surgery? What points should influence the practitioner in choosing the type of anæsthetic to be used? The practitioner may have little choice because he is working alone, and it may be impossible or highly inconvenient for him to obtain the assistance of a colleague to anæsthetize the patient. He must then adopt one of three alternatives:—(1) He may do the operation without an anæsthetic: a course of action justified and possible only in a limited group of cases, for example, suture of simple wounds, incision of acute abscesses. (2) He may administer a general or an intravenous anæsthetic himself and then perform the operation; again a line of action justifiable only in emergency cases. Unless he has the assistance of a trained nurse to look after the unconscious patient, his attention will inevitably be divided between the anæsthetic and the operation. (3) He may use local analgesia: a method which has the great advantage that it can be carried out efficiently single-handed.

it must not interact with adrenaline, which is usually added to the anæsthetic solution. No known drug completely satisfies all these criteria, but two drugs come sufficiently near doing so to form useful and reliable local analgesics—these are procaine and nupercaine.

To deal with *nupercaine* first, it may be stated that, in this country at any rate, it is not widely used for local analgesia, but is used for spinal analgesia and for surface analgesia. It has two main disadvantages: it is readily decomposed by alkalis, so that all glass-ware, needles, and the like, with which it is brought into contact, must be sterilized in alkali-free water; and it is toxic, although in the concentrations used for local analgesia, 1:1500 to 1:2000, this is not a serious matter.

Procaine, on the other hand, is widely used, and is probably still the most generally useful drug for the purpose. It is known by a number of names, some proprietary, for example, novocaine, planocaine, kerocaine, neocaine. It satisfies most of the required criteria—soluble in water, withstands boiling, even repeated boiling, non-toxic in strength and quantity used, reliable, and gives analgesia for about an hour. It has one disadvantage in that it produces vasodilatation, and it is therefore combined with adrenaline. The latter, by its vasoconstrictor action, enhances the analgesic effect of procaine and delays its absorption, so prolonging its effects and giving time for its detoxification by the liver. Adrenaline also diminishes bleeding from the wound.

For local infiltration, procaine is used in a strength of $\frac{1}{2}$ per cent. or 1 per cent., and in these strengths the average safe total quantity for a healthy adult is respectively 300 c.cm. and 125 c.cm.—ample quantities for any minor operation. Concentrations of 1 per cent. or 2 per cent. are suitable for nerve-blocking, the safe quantity of the 2 per cent. solution being 40 c.cm. Although procaine solutions keep well and can be reboiled, it is better, so far as possible, to use recently prepared solutions. These may be prepared readily by the practitioner himself immediately before operation, by dissolving procaine powder or tablets in sterile saline. The powder can be obtained in capsules, each containing 0.5 gm. The contents from one capsule dissolved in 100 c.cm. of normal saline give a $\frac{1}{2}$ per cent. solution. Adrenaline solution (1:1000) should be added to the anæsthetic solution before use in a strength of five to ten drops per 100 c.cm. of solution.

The *instruments* necessary for local analgesia are few and simple: a record or other glass-barrelled syringe of 10 c.cm. capacity, preferably with an eccentric nozzle, is suitable for minor work, and one or two needles of different sizes. A very fine hypodermic needle should be used for producing the intradermal wheals, and one or two larger needles, about 5 cm. and 8 cm. in length, for infiltrating the deeper tissues. The syringe and needles, a small medicine glass or bowl, and a measuring glass if the practitioner is preparing his own solution, should be sterilized by boiling.

Premedication.—As has been mentioned, some preoperative sedative

with the administration, such as accidental intra-arterial injection and injection of the drug into the tissues, and the dangers due to the drug itself in such conditions as liver and kidney disease, shock, and cardiac disease.

LOCAL ANALGESIA

Local analgesia, extensively used in some countries for major surgery, in this country finds its greatest sphere of usefulness in minor surgery. It has many advantages over general anæsthesia in this field. It can be used by the practitioner working single-handed. It requires a minimum of apparatus. When used in moderate quantity and correct strength, it is effective in producing analgesia. It has no undesirable after-effects and no period of recovery is necessary after its administration, so that the patient can leave hospital or surgery and go home immediately after the operation.

On the other hand, local analgesia is unsuitable for use in children and, unless combined with a preoperative sedative, in patients who are unduly apprehensive. It is unsatisfactory if the operation area is the site of scar tissue formation. Local analgesia by injection should not be used when infective lesions are being dealt with. Finally, if there is a possibility that a more extensive operation may be required, general anæsthesia should be preferred.

Local analgesia may for practical purposes be obtained in one of three ways:—(a) by the application of cold; (b) by the injection of a drug into the tissues; and (c) by surface application of such a drug.

Local analgesia by freezing.—The cold or freezing method has a very limited application. It is used only for making an incision through the skin to drain a superficial abscess. Some would say that the method should never be used, on the grounds that the analgesia is effective for only a very short time and is often incomplete, and that the pain produced by freezing the tissues is as bad as the pain produced by an incision. The drug used to produce analgesia by freezing is ethyl chloride. It is available in special tubes with a fine escape nozzle. The warmth of the operator's hand is sufficient to cause vaporization, and so to raise the pressure in the tube. When the nozzle is then opened, a fine jet of ethyl chloride escapes. This jet is directed on to the proposed line of incision and played along this line until the tissues suddenly blanch. The incision is then quickly made. There is considerable after-pain as the tissues "thaw out"—a not inconsiderable disadvantage.

Local analgesia by injection of a drug.—The method consists essentially in the introduction into the tissues of a drug which paralyses the sensory nerves or nerve-endings without first irritating them and so causing pain. Such a drug, in the concentration used, must not damage other tissues nor produce toxic effects; it must be soluble in water and must be capable of sterilization by boiling; it must be reliable in its action, and its effects must be temporary but sufficiently prolonged to give time for the operation, and

it must not interact with adrenaline, which is usually added to the anæsthetic solution. No known drug completely satisfies all these criteria, but two drugs come sufficiently near doing so to form useful and reliable local analgesics—these are procaine and nupercaine.

To deal with *nupercaine* first, it may be stated that, in this country at any rate, it is not widely used for local analgesia, but is used for spinal analgesia and for surface analgesia. It has two main disadvantages: it is readily decomposed by alkalis, so that all glass-ware, needles, and the like, with which it is brought into contact, must be sterilized in alkali-free water; and it is toxic, although in the concentrations used for local analgesia, 1:1500 to 1:2000, this is not a serious matter.

Procaine, on the other hand, is widely used, and is probably still the most generally useful drug for the purpose. It is known by a number of names, some proprietary, for example, novocaine, planocaine, kerocaine, neocaine. It satisfies most of the required criteria—soluble in water, withstands boiling, even repeated boiling, non-toxic in strength and quantity used, reliable, and gives analgesia for about an hour. It has one disadvantage in that it produces vasodilatation, and it is therefore combined with adrenaline. The latter, by its vasoconstrictor action, enhances the analgesic effect of procaine and delays its absorption, so prolonging its effects and giving time for its detoxification by the liver. Adrenaline also diminishes bleeding from the wound.

For local infiltration, procaine is used in a strength of $\frac{1}{2}$ per cent. or 1 per cent., and in these strengths the average safe total quantity for a healthy adult is respectively 300 c.cm. and 125 c.cm.—ample quantities for any minor operation. Concentrations of 1 per cent. or 2 per cent. are suitable for nerve-blocking, the safe quantity of the 2 per cent. solution being 40 c.cm. Although procaine solutions keep well and can be reboiled, it is better, so far as possible, to use recently prepared solutions. These may be prepared readily by the practitioner himself immediately before operation, by dissolving procaine powder or tablets in sterile saline. The powder can be obtained in capsules, each containing 0.5 gm. The contents from one capsule dissolved in 100 c.cm. of normal saline give a $\frac{1}{2}$ per cent. solution. Adrenaline solution (1:1000) should be added to the anæsthetic solution before use in a strength of five to ten drops per 100 c.cm. of solution.

The *instruments* necessary for local analgesia are few and simple: a record or other glass-barrelled syringe of 10 c.cm. capacity, preferably with an eccentric nozzle, is suitable for minor work, and one or two needles of different sizes. A very fine hypodermic needle should be used for producing the intradermal wheals, and one or two larger needles, about 5 cm. and 8 cm. in length, for infiltrating the deeper tissues. The syringe and needles, a small medicine glass or bowl, and a measuring glass if the practitioner is preparing his own solution, should be sterilized by boiling.

Premedication.—As has been mentioned, some preoperative sedative

may be desirable in apprehensive patients. A small dose of morphine or morphine and scopolamine may be used on occasion, or one of the barbiturates may be more suitable and convenient. The reader is referred to the article on "Pre-anæsthetic Medication" for a fuller discussion of this subject.

THE TECHNIQUE OF LOCAL ANALGESIA

Local infiltration.—The principle of this method is to infiltrate the tissues in the operation area and so paralyse the sensory nerve-endings.

An adequate area of skin around the site of the lesion having been shaved and prepared with antiseptic, one or more intradermal wheals are raised a short distance from the site of the lesion. This is done by inserting the point of a fine needle very obliquely into, but not through, the skin, and injecting a few drops of the anæsthetic solution. This raises a white wheal about 1 cm. in diameter which is immediately anæsthetic. One of the longer needles is now attached to the syringe, pushed through the insensitive wheal and then slowly advanced just deep to the skin, the anæsthetic being injected all the time (fig. 1). The danger of intravenous injection must always be guarded against by attention to this point in technique and by the aspiration test. The line of proposed incision having been infiltrated in this way, the needle is almost withdrawn and the injection repeated fan-wise on either side. If a sufficient area has not been dealt with through the first wheal, the process can be repeated through other wheals suitably placed. Depending upon the depth of the lesion, the deeper tissues may have to be similarly infiltrated.

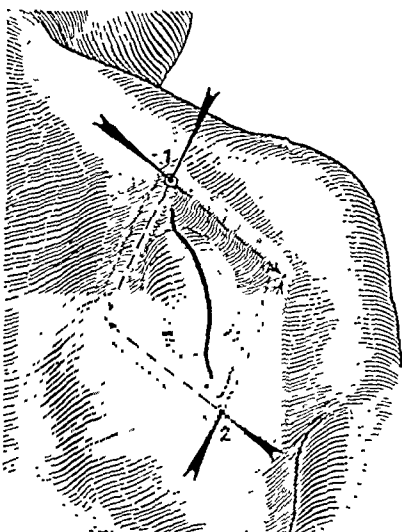


FIG. 2.—Field-block for removal of a lipoma.—Intradermal wheals are raised, (1) and (2), a little beyond the extremities of the proposed incision. Injections are made in the lines of the arrows.

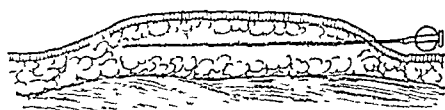


FIG. 1.—Subcutaneous infiltration.

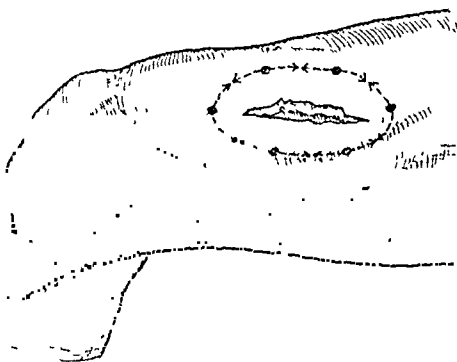


FIG. 3.—Field-block for cleansing and suture of a wound.—Wheals are raised at the sites of the black dots. The arrows indicate the direction of the needle.

Field-block.—In this method the anæsthetic is not injected into the tissues at the site of operation, but instead is injected around the site in planes

perpendicular or oblique to the surface so as to surround the operation area with walls of analgesia. The tissues within the walls are thus rendered insensitive (fig. 2 and 3).

Nerve-block.—The principle underlying this method is to deposit the anæsthetic fluid in the immediate vicinity of the nerves supplying the area of operation. Here the anæsthetic acts on the nerves instead of on the terminal twigs and sensory nerve-endings as in infiltration anæsthesia. In minor surgery this method is used for anæsthetizing fingers and toes (fig. 4).

Whatever method is used, success will be obtained only if strict attention is paid to the following points:—(1) Adequate time must be allowed for the anæsthetic to take effect—at least five minutes after completion of the injection; (2) the utmost gentleness is necessary; it must always be remembered that the patient is conscious and that only a small part of the body is anæsthetized; (3) the operative interference must be confined within the anæsthetized area.

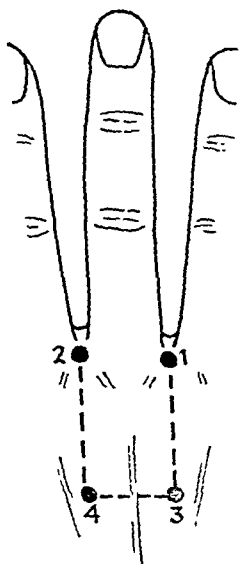


FIG. 4.—Anæsthetizing a finger.—Through wheals (1) and (2) injections are made so as to deposit a ring of anæsthetic round the base of the finger. To anæsthetize the tissues around the metacarpal head and the joint, interosseous injections are made through (3) and (4), and subcutaneous infiltration along the dotted lines.

SURFACE ANALGESIA

This method is used only in the eye, the nose, the larynx, and the urethra. A 4 per cent. solution of cocaine hydrochloride is used in the conjunctiva. Stronger solutions of cocaine, for example, 10 per cent., are used intranasally. Some degree of anæsthesia can be obtained for the passage of urethral bougies, by instilling some 10 c.cm. of 4 per cent. procaine or 1:1000 nupercaine into the urethra and maintaining the anæsthetic in contact with the mucous membrane for some minutes.

EXAMPLES OF THE USE OF LOCAL ANALGESIA IN MINOR SURGICAL CONDITIONS

Cleansing and suture of minor accidental wounds; removal of small superficially placed foreign bodies, for example, splinters of wood, fish-bones. The method of field-block can be used with advantage in such cases.

Removal of superficial tumours, such as lipomas, hæmangiomas, warts or sebaceous cysts, and of a lymph node for biopsy. Local infiltration or field-block is appropriate in such cases.

Operations on the fingers and toes, such as accidental wounds, affections of the nails, amputations. Analgesia of a digit is readily achieved by the method of nerve-block.

A fine needle is used and is inserted vertical to the surface, on the dorsal aspect to one side of the base of the digit. As soon as the point of the needle is through the skin, injection of 1 per cent. procaine is begun and is continued as the needle is pushed towards the palm/sole. The operator's left forefinger placed on the palm/sole controls the depth of the injection and prevents the surgeon from penetrating the palmar/plantar skin. The injection is repeated through another puncture on the opposite side of the base of the digit. A ring of anæsthetic is thus placed round the base of the digit, bathing all the digital nerves and so rendering the whole digit anæsthetic. Anæsthesia spreads from the base to the tip, and adequate time must be allowed for this, especially if the operation is on the distal part of the finger or toe.

If complete amputation of a digit is contemplated, the anæsthesia must be carried more proximally by infiltrating the interosseous spaces between the metacarpal/metatarsal bones and a corresponding area of skin on the dorsum (fig. 4).

Ligature of varicose veins.—Simple infiltration of the line of incision, of a small area of skin around, and of the subcutaneous tissues is adequate for this operation.

Paracentesis.—In removing fluid for diagnostic or therapeutic purposes from the pleural cavity, the peritoneal cavity, the spinal theca (lumbar puncture), or the tunica vaginalis testis (hydrocele), local anæsthesia should be used. A skin wheal is made and a little anæsthetic solution (1 per cent.) deposited in the deeper tissues in the line to be taken by the aspirating needle.

Ano-rectal conditions.—The thrombus which constitutes the hæmatoma ani, or acute thrombosed external pile, is easily removed under local anæsthesia, by simple infiltration of the overlying peri-anal skin.

The therapeutic use of one of the long-acting oil-soluble anæsthetics, such as *proctocaine*, in the treatment of anal fissure may be referred to briefly.

The needle having been passed through the skin 1 in. behind the anus, 5 to 10 c.cm. of the oily solution are injected deeply into the sphincter muscles on each side of the anus and under the fissure, the position of the needle being controlled by the surgeon's left forefinger in the anal canal.

The anæsthetic produces immediate relief from pain and sphincter spasm, and the effect may last for one to two weeks, which allows the fissure to heal.

Local analgesia for sprains.—The infiltration of a sprained ligament with a local analgesic often produces strikingly beneficial effects. Five to ten cubic centimetres of 2 per cent. procaine are injected into the ligament at the point of maximum tenderness. Immediate relief is usually obtained, but the patient should be warned that the pain may recur temporarily in an aggravated form in a few hours, before finally disappearing in a day or two. If, after a few days, pain is still present, the injection may be repeated.

PRE-ANÆSTHETIC MEDICATION

By W. D. WYLIE, M.B., B.CHIR., M.R.C.P., D.A.

Anæsthetist, St. Thomas's Hospital.

PRE-ANÆSTHETIC medication has been used for many years to allay the fear of operation and to prevent the excessive secretions caused by ether. These are the two most important and most obvious uses for pre-anæsthetic drugs, but nowadays few anæsthetists would be satisfied that they constitute the only indications for their use. It is intended here to formulate four principles which illustrate the scientific and clinical bases for pre-medication; then to discuss in general the drugs commonly used for this purpose, adding those points which are considered of importance when dealing with children and the aged. Finally, a chart is offered as a general guide for the premedication of the average case.

GENERAL PRINCIPLES

Sedation.—The relief of mental stress and the production of drowsiness and amnesia are of prime importance. The time of the patient's greatest fear is in the immediate preoperative period while waiting in the anæsthetic room or operating theatre. But the preceding twenty-four hours are important and in exceptional cases, such as those with thyrotoxicosis, sedation may be necessary for an even longer period while the patient is being prepared for operation.

Prevention of excessive salivary and bronchial secretions.—This is essential when an irritating anæsthetic agent such as ether is to be used but, nevertheless, is a safeguard whatever agent is intended. It offers some protection against already existing secretions causing bronchial obstruction when the cough reflex is removed, and allows a change to an irritating agent to be made without worry, should this prove necessary.

Lowering of the basal metabolic rate.—It is the aim of all anæsthetists to achieve the best operating conditions with the minimum of anæsthetic agent or agents. In this connexion the simple action of all anæsthetic agents and central depressants in lowering the basal metabolic rate is of great importance. A given quantity of a weak but harmless agent such as nitrous oxide will produce a limited level of anæsthesia in a healthy adult. A small dose of morphine given one hour before the operation will lower the basal metabolic rate without producing anæsthesia, but will allow the same quantity of nitrous oxide to produce a slightly greater depth of anæsthesia. This increased depth may make all the difference between a quiet and a stormy anæsthetic for a small but painful minor operation. The real merits of this premedication are better appreciated in those patients who start with an abnormally high basal metabolic rate, either from fear or disease, and in whom the use of an innocuous agent such as nitrous oxide is preferable.

A fine needle is used and is inserted vertical to the surface, on the dorsal aspect to one side of the base of the digit. As soon as the point of the needle is through the skin, injection of 1 per cent. procaine is begun and is continued as the needle is pushed towards the palm/sole. The operator's left forefinger placed on the palm/sole controls the depth of the injection and prevents the surgeon from penetrating the palmar/plantar skin. The injection is repeated through another puncture on the opposite side of the base of the digit. A ring of anæsthetic is thus placed round the base of the digit, bathing all the digital nerves and so rendering the whole digit anæsthetic. Anæsthesia spreads from the base to the tip, and adequate time must be allowed for this, especially if the operation is on the distal part of the finger or toe.

If complete amputation of a digit is contemplated, the anæsthesia must be carried more proximally by infiltrating the interosseous spaces between the metacarpal/metatarsal bones and a corresponding area of skin on the dorsum (fig. 4).

Ligature of varicose veins.—Simple infiltration of the line of incision, of a small area of skin around, and of the subcutaneous tissues is adequate for this operation.

Paracentesis.—In removing fluid for diagnostic or therapeutic purposes from the pleural cavity, the peritoneal cavity, the spinal theca (lumbar puncture), or the tunica vaginalis testis (hydrocele), local anæsthesia should be used. A skin wheal is made and a little anæsthetic solution (1 per cent.) deposited in the deeper tissues in the line to be taken by the aspirating needle.

Ano-rectal conditions.—The thrombus which constitutes the hæmatoma ani, or acute thrombosed external pile, is easily removed under local anæsthesia, by simple infiltration of the overlying peri-anal skin.

The therapeutic use of one of the long-acting oil-soluble anæsthetics, such as *proctocaine*, in the treatment of anal fissure may be referred to briefly.

The needle having been passed through the skin 1 in. behind the anus, 5 to 10 c.cm. of the oily solution are injected deeply into the sphincter muscles on each side of the anus and under the fissure, the position of the needle being controlled by the surgeon's left forefinger in the anal canal.

The anæsthetic produces immediate relief from pain and sphincter spasm, and the effect may last for one to two weeks, which allows the fissure to heal.

Local analgesia for sprains.—The infiltration of a sprained ligament with a local analgesic often produces strikingly beneficial effects. Five to ten cubic centimetres of 2 per cent. procaine are injected into the ligament at the point of maximum tenderness. Immediate relief is usually obtained, but the patient should be warned that the pain may recur temporarily in an aggravated form in a few hours, before finally disappearing in a day or two. If, after a few days, pain is still present, the injection may be repeated.

reasons there is much to be said in favour of scopolamine (*l*-rotatory hyoscine hydrobromide) which, whilst preventing the excessive flow of secretions, possesses no unfortunate side-reactions in correct dosage and has a central depressant action which produces sedation and amnesia. In children, secretory activity, which tends to be more excessive than in adults, is not well controlled by scopolamine and it is probable that a small dose of atropine is best in these cases. Scopolamine is given to adults in a dosage of 1/150 of a grain (0.43 mgm.).

Combinations such as have been described are usually given hypodermically one hour before operation, but if the patient should arrive in the operating theatre without having received any premedication, they can be given intravenously. On these occasions the same dose should be used but in a somewhat more dilute solution, and two or three minutes should be taken for the injection.

Barbiturates.—These drugs may be classified on the basis of their relative periods of action. Phenobarbitone, which acts for a long period, is best used to settle down the worried and frightened patient who is being prepared for operation over some few days. A dosage of $\frac{1}{2}$ a grain (32 mgm.) b.d., or 1 grain (65 mgm.) b.d., will prove satisfactory in most cases.

Pentobarbital sodium or nembutal, which has a medium period of action, is valuable for producing a good night's sleep before the operation. Two other proprietary drugs are worth mentioning in this respect, as it is often found that a patient has an individual tolerance to one, particularly if it has been used previously. They are seconal (sodium propylmethylcarbinyllallyl-barbiturate) and soneryl (butobarbital sodium). A dosage of $1\frac{1}{2}$ grains (0.1 gm.) of any of these given last thing at night will usually suffice for patients unaccustomed to sedation, whilst 3 grains (0.2 gm) will be adequate for more resistant and more frightened patients. This class of barbiturates is also useful for premedication in the immediate preoperative period as a substitute for opium derivatives. It should not be necessary to exceed a dosage of 3 grains (0.2 gm) for adults. The dosage for children is discussed later.

In exceptional cases the use of barbiturates in the immediate preoperative period leads to excitement in the immediate postoperative period. This is rarely a manifestation of idiosyncrasy to the particular barbiturate, but is commonly due to the fact that the patient has no relief from the pain of operation, having had no preoperative opiate. For patients suffering from pain before operation, and in whom it is particularly desired to avoid the use of opiates, a combination of barbiturate and simple analgesic is often satisfactory: sodium barbitone, $7\frac{1}{2}$ grains (0.5 gm.), and acetylsalicylic acid, 5 grains (0.32 gm.), is a useful example.

BASAL NARCOTICS

Certain drugs are used to produce sleep and unconsciousness without surgical anæsthesia in the preoperative period. Such drugs are known as

With such an agent no anæsthesia will be achieved without the use of a premedicant.

Prevention of certain side-effects.—Many anæsthetic drugs, and indeed the stimuli of both anæsthetic and surgical procedures, possess toxic side-effects or initiate reflexes which may have unfortunate sequelæ for the patient. The toxic effects of local anæsthetics are less likely to occur if a barbiturate has been administered to the patient before operation (Barbour, 1936). The passage of an endotracheal tube causes stimulation of the parasympathetic nervous system which may in turn initiate changes in the cardiovascular system. These are less likely to occur if the patient has been given a drug of the atropine class (Reid and Brace, 1940).

DRUGS

A number of drugs are in common use as premedicants, and in practice it is found that each often covers one or more principles. It should not be forgotten, however, that a visit by the anæsthetist to the patient before the operation is often of far greater value than any sedative drug. Not only does it enable the anæsthetist to allay the patient's fears, but it also allows him to assess the patient's condition and so decide upon the correct premedication in relation to this, and the anæsthetic and technique to be used.

Opium derivatives.—Morphine is still the most commonly used sedative in the preoperative period and has an excellent effect on the basal metabolic rate, whilst also reducing secretory activity. It is invaluable when there is much pain. It is liable to cause sickness in some people and for this reason omnopon, which is a mixture of all the alkaloids of opium, is preferred by many. Morphine $\frac{1}{2}$ of a grain (11 mgm.) is equivalent to omnopon $\frac{1}{2}$ of a grain (22 mgm.), and to achieve the best results this dose combined with atropine or scopolamine, as described below, should be given hypodermically to average-sized adults one hour before operation. When prescribing such premedication it is well to bear in mind what anæsthetic agent it is intended to use later, as the relative respiratory depression so caused may make administration difficult. In such cases morphine, $\frac{1}{2}$ of a grain (8 mgm.), or omnopon, $\frac{1}{2}$ of a grain (11 mgm.), may prove more satisfactory, and indeed there are some who prefer no opiate at all. However, if sedation is necessary a barbiturate may be substituted.

Atropine and hyoscine.—Atropine is prescribed for adults in a dosage of $\frac{1}{100}$ of a grain (0.65 mgm.) to reduce the secretion of saliva and mucus. It is said that atropine has a respiratory stimulant effect which tends to offset the depression of morphine. Whether this be true or not, it definitely has a stimulant action on the basal metabolic rate, and this increases the pulse rate and oxygen consumption of the patient. These facts are deterrents to its use in full dosage in toxic and sick patients. Moreover, its powerful effect is liable to cause excessive dehydration and to produce a sticky and tenacious mucus which may predispose to postoperative pulmonary complications. It may also cause a considerable rise in temperature. For these

Paraldehyde.—Paraldehyde is a safe basal narcotic which requires little preparation. It has a most unpleasant smell and occasionally is uncertain in its action, producing excitement rather than sedation. It is prepared as a 10 per cent. solution in normal saline and is given per rectum in a similar manner to bromethol. The dosage is estimated at 60 minims (3.5 c.cm.) per stone body weight, with a maximum of 480 minims (28 c.cm.). Within the limits of the dosage described it is unlikely that complete unconsciousness will be produced in adults, but it is particularly useful for frightened children as they can be put to sleep very easily. Moreover, it does not produce either respiratory depression or a fall in blood pressure (Rowbotham, 1931).

CHILDREN

Unless in pain, young children rarely need sedation the night before operation, and the necessity to allay the fears of operation should not arise if they have been properly handled and not told of the impending event. Older children from about ten to fifteen years are often apprehensive and a small dose of barbiturate may be very helpful. Seconal, $1\frac{1}{2}$ grains (0.1 gm.), will be satisfactory, but every attempt should be made to judge the dose according to size and age.

In the immediate preoperative period it is desirable when possible, both from the point of view of the children and of the anæsthetist, who desires a pleasant and equable induction, that they should arrive in the anæsthetic room asleep. Seconal, in a dosage of $\frac{1}{2}$ a grain (32 mgm.) per 10 pounds body weight, or nembutal, in a dosage of $\frac{1}{2}$ a grain (32 mgm.) per stone body weight, and each with a maximum of 3 grains (0.2 gm.) will achieve this if given one-and-a-half hours before operation. The powder should be removed from the capsules and mixed with jam. When asleep, a hypodermic injection of $1/100$ of a grain (0.65 mgm.) of atropine may be given without any disturbance. Older children may not sleep soundly but will certainly be more cooperative than without sedation. If preferred, older children from ten to fifteen years may be given $1/12$ of a grain (5.4 mgm.) of morphine and $1/100$ of a grain (0.65 mgm.) of atropine one hour before operation. Children below the age of eighteen months are probably most safely premedicated with $1/150$ of a grain (0.43 mgm.) of atropine given half an hour before operation and left unsedated. The memory of the event will be very short. Scopolamine is very likely to produce restlessness when given to children in a dosage adequate to prevent excessive secretions and is therefore best avoided.

Occasionally it may be impossible to make small children take oral drugs, and in such cases it is useful to be able to induce basal narcosis by rectal methods. Paraldehyde may be used as already described, but this leaves an unpleasant smell for some time. Nembutal suppositories are very satisfactory. The dose should be estimated at $\frac{1}{2}$ a grain (32 mgm.) per stone body weight with a maximum of 3 grains (0.2 gm.), and the sup-

basal narcotics. They combine the advantages of some of the previously discussed premedicants but go further, in that they completely obviate any possibility of fear on the part of the patient after they have been given. Their disadvantages are that there is no routine dosage and for each case this must be worked out exactly; they involve more time in their preparation and administration; increased nursing care is necessitated after operation, and cumulative effects with other agents may occur. They are most commonly used for special cases and, since they have no effect on secretory activity, are usually followed by a hypodermic injection of atropine or scopolamine.

Whatever method of basal narcosis is used it must always be remembered that when unconscious the patient must be looked after as though under full surgical anæsthesia.

Bromethol.—Bromethol or avertin is a white powder. It is supplied dissolved in amylene hydrate as a clear solution, 1 c.cm. of which contains 1 gm. It is given per rectum and is made up in distilled water to a strength of 2½ per cent. The exact dosage is calculated according to the weight of the patient: 0.1 c.cm. of the bromethol fluid should be given for each kilogram of body weight. The final solution in distilled water should always be made up freshly just before use, and should be tested with the congo red indicator for the presence of hydrobromic acid. If this is present the indicator will turn blue and the solution must be discarded. The solution should be given slowly over ten minutes and it should be started twenty minutes before operation.

Nowadays, bromethol is used less frequently than ever before, since it is rarely that a patient cannot be given an intravenous injection of thiopentone. In certain cases of thyrotoxicosis, however, there still remains an indication for its use when even an injection might upset the patient and it is preferable to produce unconsciousness without the patient's foreknowledge. Moreover, there is some evidence to suggest that bromethol and thyroxine are antagonistic (Carlton, 1929). Bromethol produces some respiratory depression and a slight fall in the blood pressure; factors which should be remembered when it is used.

Thiopentone sodium.—Thiopentone sodium or pentothal, the best known of the short-acting barbiturates, is most commonly used as an anæsthetic agent, but may, by regulating the dosage, be used as a basal narcotic. It may be given intravenously or per rectum. In the former event it should be made up in a 5 per cent. solution by dissolving 0.5 gm. in 10 c.cm. of sterile distilled water. It is administered to the patient in bed by the anæsthetist and is injected slowly until unconsciousness just occurs. Seldom should more than 0.5 gm. be necessary to produce sufficient narcosis to enable the patient to be transferred to the operating theatre, and in many cases less will suffice. For rectal use, 1 gm. per 50 pounds of body weight is dissolved in an ounce of distilled water (Weinstein, 1939). This solution should be run slowly into the rectum thirty minutes before operation.

ANALGESIA AND ANÆSTHESIA IN OBSTETRICS

By G. C. STEEL, M.R.C.S., L.R.C.P., D.A.

Anæsthetist, Chelsea Hospital for Women, and Queen Charlotte's Hospital.

THE problem of the relief of pain in childbirth is one for which a satisfactory solution has yet to be found. The complicating factors are legion, the principal ones being that two lives are involved, and that the degree of justification for the use of any dangerous form of anæsthesia in midwifery cannot be the same as, for example, in the case of an abdominal catastrophe. In the latter instance, an anæsthetic is being given to allow a life-saving surgical procedure to be undertaken: in the former to afford relief from pain which can admittedly be an overwhelming agony, but which does not generally constitute an immediate and direct threat to life. Provided, however, that a reasonable amount of skill and judgment be exercised, there is but slight risk to mother or child in the use of modern drugs.

The drugs which are used may be classed as those given orally, by inhalation, rectally, and by injection; finally, those which are used for some form or another of nerve-block. Their purpose is twofold: to produce analgesia during the first and second stages, and to produce anæsthesia, when necessary, for the actual delivery or for obstetrical operations. There are certain criteria against which every such drug must be judged:—

- (1) It should act promptly and effectively.
- (2) It should exercise the minimal toxic or depressant effect on mother and fœtus.
- (3) It should be reasonably easy to administer as well as being transportable and inexpensive.
- (4) It should not impair uterine contractility.
- (5) Its action should be readily convertible from that of an analgesic to that of an anæsthetic, and *vice versa*.

Within the framework of these conditions, the practitioner's choice of method should be influenced by:—

- (a) The nature of each case, and the temperament of the mother.
- (b) His own experience of any particular technique, and the degree of success that he feels that he gets with it.
- (c) The sleep requirements of the patient. All too often this important factor is overlooked, and the patient, in the discomfort of the early stages of labour, is allowed to lie sleepless through the night. With the coming of day she faces a physical effort comparable to that of a hard cross-country run, already tired instead of being refreshed and calm.

Whatever method be used, its effective value will be greatly increased or diminished by the patient's mental approach to labour, and much can

pository should be inserted three hours before the operation (Jarman, 1936).

THE AGED

There is little concerning the aged to suggest a move away from the principles already recorded, as the dosage should be assessed with a view to the general physical state and age. In general, the basal metabolic rate tends to fall after twenty-five years of age, and so in those over sixty it is likely that a smaller dose of opiate will be needed. At this age, too, scopolamine is often poorly tolerated and it is safer to use atropine instead.

DISCUSSION

Every case should ideally be assessed on its own merits in relation to the physical and mental state, the operation to be performed, and the particular type and mode of anæsthesia to be used. In outlining the principles and the drugs which are commonly used for premedication these points have been discussed generally. Mention has not been made of particular operations or diseases, since a proper understanding will enable the correct dosage and the correct drug to be used. Thus, for example, it should not be necessary to stress that it is unwise to give atropine to a case of thyrotoxicosis as it will exacerbate the existing disease. It is noteworthy, however, that many anæsthetists have a general and easily remembered chart for premedication of the average case. The following guide is an arbitrary one but it may well suit most requirements for general use.

Children: Aged 0-18 months: Atropine, $1/150$ of a grain (0.43 mgm.) half an hour before operation.

Aged 18 months-10 years. Nembutal, $\frac{1}{2}$ a grain (32 mgm.) per stone body weight, to a maximum of 3 grains (0.2 gm.), one-and-a-half hours before operation, followed by $1/100$ of a grain (0.65 mgm.) of atropine half an hour before operation.

Aged 10-15 years. As above, or morphine, $1/12$ of a grain (5.4 mgm.), and atropine, $1/100$ of a grain (0.65 mgm.), one hour before operation.

Adults: Aged 15-60 years. Morphine, $1/6$ of a grain (11 mgm.), and scopolamine, $1/150$ of a grain (0.43 mgm.), one hour before operation.

Over 60 years. Morphine, $1/8$ of a grain (8 mgm.), and atropine, $1/100$ of a grain (0.65 mgm.), one hour before operation.

SUMMARY

- (1) The principles underlying premedication are briefly discussed.
- (2) The most commonly used drugs are described with their dosage.
- (3) A guide is offered for the premedication of the average case.

References

- Barbour, H. C. (1936): *Amer. J. Surg.*, 34, 441.
 Carlton, H. (1929): *Proc. Roy. Soc. Med.*, 23, 106.
 Jarman, R. (1936): *Brit. med. J.*, i, 236.
 Reid, L. C., and Brace, D. E. (1940): *Surg. Gynec. Obst.*, 70, 157.
 Rowbotham, S. (1931): *Brit. med. J.*, ii, 693.
 Weinstein, M. L. (1939): *Anesth. and Analg.*, 18, 221.

Gas and oxygen.—The success of gas and oxygen depends both upon the patience and experience of the anæsthetist, and also upon the cooperation of the patient. Given these essentials, it is hard to improve on this method, and no apology is made for reiterating the details that make for success. At the beginning, the anæsthetist should explain to the patient that the gas will send her into a light sleep for the duration of the contraction; that it is essential that she should tell him as soon as she feels the warning of an approaching pain, rather than wait until it is firmly established; and that although she will experience almost complete relief of pain, she may still be able to hear what is being said to her.

As soon as the warning of the contraction is felt, three breaths of pure gas should be given, and oxygen then run in. The percentage of oxygen should be the maximum compatible with adequate relief of pain, and should never fall below 10 per cent. During the second stage she should be told to take three or four deep breaths, then at the end of an inspiration to hold her breath and to bear down.

Gas and oxygen will often suffice for the delivery, but should this prove difficult, then it is better to add a small amount of cyclopropane, trilene, or ether, rather than lower the oxygen percentage to a level that will cause maternal and foetal anoxæmia.

Gas and air.—The self-administration of gas and air under the supervision of a midwife is a useful alternative when gas and oxygen is impracticable. Minnitt's machine and the Jecta apparatus are both to be recommended. The latter utilizes the jet principle to attain the necessary mixture of gas and air. The gas passes through a tapered jet at high velocity, and the negative pressure thus created sucks in air from a side channel. Whatever apparatus is used, the chances of success are greatly enhanced if the whole procedure is carefully and painstakingly explained to the patient. This should be done as early as possible, rather than when the patient is well on in labour and distracted by the concomitant hurly-burly.

Meticulous attention should be paid to such details as the fitting of the mask on the face; to the efficient stopping-up of the safety vent by the patient's finger; and to encouraging her to try to time the inhalation of gas so as to "beat the pain". The desirability of antenatal instruction in the use of the apparatus has been emphasized by Minnitt (1947).

The disadvantage of gas and air is that it is not always adequate for the more painful moments of labour.

Trilene.—Trichlorethylene is a relatively weak and unstable anæsthetic, but has marked analgesic and amnesic properties which render it a most useful drug in midwifery. It is particularly effective for supplementing gas and air or oxygen when this proves inadequate for delivery or forceps: the transition from analgesia to anæsthesia is smooth and simple.

For self-administration throughout labour, either the Freedman or the Trilite inhaler, both of which give a fixed concentration, can be used. In addition, there are the Hyatt-Siebe-Gorman and the Cyprane inhalers. In each of these the concentration can be varied by means of an adjustable mechanism which is locked in any given position with a key kept by the medical attendant. The Cyprane model has the vapourizing chamber attached directly to the facepiece: this means that

be done to allay the fears so easily built up around the tea-table and in the antenatal waiting room.

DRUGS GIVEN BY MOUTH

These include the time-honoured mixture of potassium bromide and chloral. Whilst it has the advantage of being one of the safest forms of treatment, in pharmacological dosage it can only have a very mild sedative effect. Occasionally slight nausea or a bromide rash may occur.

The barbiturates, which are classed as heavy, medium, or light according to whether they are slowly or rapidly broken down, have had many advocates. The present position is that a rather guarded view is taken of their use, for they are transplacental in action and the heavy ones may result in sleepy babies when given late in labour. Nevertheless, there still remains a niche for them in midwifery, provided that they are used with discretion.

For the production of sleep in the early stages of what promises to be a prolonged labour, one of the heavy or medium groups may be used. The practitioner's own experience of these drugs is his best guide in choosing which one to use.

Many of the light group have been used to produce analgesia or to supplement the efficacy of gas and air. The more modern drugs, such as pethidine and trilene, are tending to replace the barbiturates in this respect, but those who have gained considerable experience with the latter may well feel disinclined to desert their trusted favourites. Pentothal sodium, 3 grains (0.2 gm.), repeated at half- to one-hourly intervals, with maximum dosage of 20 grains (1.3 gm.); pentothal acid, 6 to 8 grains (0.4 to 0.52 gm.), repeat doses of 4 to 6 grains (0.25 to 0.4 gm.) being given at half- to three-quarter-hour intervals, total dosage 25 to 35 grains (1.6 to 2.3 gm.); and seconal, 3 to 4½ grains (0.2 to 0.28 gm.) with repeat doses of ½ to 3 grains (32 mgm. to 0.2 gm.) at hourly intervals up to a maximum of 12 grains (0.8 gm.), have all been successfully employed.

At all times the guiding principle of timing and dosage should be that the child must not be handicapped in the first critical minutes of its independent existence by having in its system a depressant drug which it has to break down without the help of the maternal system from which it has been so recently severed.

A useful way of assessing a patient's probable reaction to a barbiturate during labour is to give her a normal sleeping dose about a fortnight before labour is due, and to see if she finds it effective or not.

DRUGS GIVEN BY INHALATION

The use of *chloroform* is on the wane, although it still has many advocates. Its portability and ease of administration render it useful for obstetrical operations when there is no equipment for giving other forms of anaesthesia: but it must always be remembered that chloroform is an extremely potent and toxic drug.

found, and no evidence of foetal respiratory depression was noted. As yet, I have had no experience of this method.

Continuous caudal analgesia, spinal nerve-blocks, and intravenous procaine injections cannot be considered as suitable for use in general practice.

GENERAL INDICATIONS

The position may be summarized as follows:—For the straightforward case, gas and oxygen or gas and air, with trilene or pethidine as possible supplementary agents are recommended. When the patient is in the early stages, and the barbiturates come into the picture; for

by sedation, morphine is indicated. In the straightforward low forceps, gas and air will suffice. When there is foetal asphyxia, but should be avoided if much distress to the patient should not be allowed. In forceps delivery, it is my custom to give oxygen until the head is delivered until the cord

for forceps delivery, but cannot be used in ciliary midwifery. On the other hand, the same risk as spinal block, and

pudendal nerve-block usually gives good results.

External version.—Gas, oxygen and ether is probably the safest combination; yet it must be admitted that chloroform stands alone in the thoroughness with which it relaxes uterine muscle.

Cæsarean section.—The planned Cæsarean section for disproportion will do well on gas and oxygen supplemented by minimal trilene or ether. Cyclopropane is also suitable. In cases of diabetes mellitus it is advisable to use some form of nerve-block which may be supplemented by a light gas and oxygen. When the mother is in poor condition, or there is foetal distress, the anæsthetist is faced with the same problem as occurs in a difficult forceps delivery under similar conditions: he must protect the mother from the shock of the obstetrical manœuvres; yet he must not depress the already enfeebled vital functions of the child. This is one of the chief reasons why some form of nerve-block has so many advocates.

Under general anæsthesia, should laryngeal spasm occur through the patient being too light, or for any other reason, the anæsthetist must devote his immediate attention to seeing that the patient is adequately oxygenated. Then, and not before, should he start to worry about the depth of anæsthesia. I believe it to be a beneficial practice to give the mother pure oxygen from the moment the delivery of the baby starts until the cord is clamped.

References

- Minnitt, R. J. (1947): "Gas and Air Analgesia," 3rd edition, London.
Tonn, G. R. (1946): *South. med. J.*, 39, 154.

during self-administration the patient has to hold the apparatus weighing $1\frac{1}{2}$ pounds, which becomes rather tiring after some time. The Siebe Gorman model has the vapourizing chamber clamped to the bed-rail, so that the patient need only hold the very light facepiece and corrugated tubing.

As yet, it is too early to make a final assessment of trilene, but it may well be that its value will be found in its employment when gas and air or oxygen prove inadequate, rather than as a form of analgesia to be employed from the beginning of labour. Two points should be mentioned: first, that trilene may not yet be administered except under the direct supervision of a qualified medical person; secondly, that it is inadvisable to give cyclopropane to a patient who has recently had trilene, owing to the necessary use of the soda-lime circuit.

DRUGS GIVEN BY INJECTION

The use of *morphine* and *scopolamine* to produce "twilight sleep" is sufficiently well known to need no comment except to say that with the advent of the safer modern drugs there is little justification for the employment of the full technique. At the same time there is a definite place for this group in midwifery; for example, in certain cases of primary uterine inertia when treatment by sedation is indicated, omnopon, $\frac{1}{3}$ of a grain (22 mgm.), or morphine, $\frac{1}{6}$ to $\frac{1}{4}$ of a grain (11 to 16 mgm.), and scopolamine, $\frac{1}{150}$ of a grain (0.43 mgm.), should be given. The patient experiences marked relief from the sharpened pain of the ineffectual contractions, and often goes to sleep, to awaken with the cervix appreciably dilated.

The warning that the full effect of the drug should not be allowed to impinge on the second stage, should always be kept in mind.

Pethidine (demerol).—This drug has been extensively used both here and in America. In action it is antispasmodic and analgesic. Originally given by mouth, it is now given by injection, generally in a dose of 100 mgm. when the pains become genuinely distressing, and repeated an hour later if necessary. Recently it has been recommended that the initial dose should be 150 mgm., in which case the repeat dose of 100 mgm. is rarely necessary.

Generally speaking, a good degree of analgesia is attained, but the effect on the course of labour is variable; sometimes the duration seems to be shortened, whilst on other occasions it may appear that uterine action is weakened.

DRUGS GIVEN PER RECTUM

Neither avertin nor paraldehyde is much used now. The constant action of any drug given by this route is liable to be upset through the patient's failure to retain it. In America, a mixture of olive oil and ether, or ether and paraldehyde in olive oil, is still used by the Gwathmey school.

More recently the rectal use of pentothal sodium has been favourably reported on (Tonn, 1946). The dosage is 1 gm. per 50 pounds body weight, and it is given when the cervix is 2 to 3 cm. dilated in multiparæ, and 3 to 4 cm. in primiparæ. A satisfactory degree of analgesia and of amnesia was

found, and no evidence of foetal respiratory depression was noted. As yet, I have had no experience of this method.

Continuous caudal analgesia, spinal nerve-blocks, and intravenous procaine injections cannot be considered as suitable for use in general practice.

GENERAL INDICATIONS

The position may be summarized as follows:—For *the straightforward case*, gas and oxygen or gas and air, with trilene or pethidine as possible supplementary agents are recommended. When the patient is in the early stages, and sleep is deemed necessary, the barbiturates come into the picture; for the treatment of primary uterine inertia by sedation, morphine is indicated.

Forceps, episiotomy, or repair.—For the straightforward low forceps, gas and oxygen with minimal trilene or ether will suffice. When there is foetal distress, cyclopropane is preferred by some, but should be avoided if much trilene has already been used. At all costs the patient should not be allowed to become cyanosed. In any case of forceps delivery, it is my custom to give the mother pure oxygen from the time the head is delivered until the cord is clamped.

Spinal nerve-block has been used for forceps delivery, but cannot be considered as being suitable for domiciliary midwifery. On the other hand, pudendal nerve-block does not carry the same risk as spinal block, and usually gives good results.

External version.—Gas, oxygen and ether is probably the safest combination; yet it must be admitted that chloroform stands alone in the thoroughness with which it relaxes uterine muscle.

Cæsarean section.—The planned Cæsarean section for disproportion will do well on gas and oxygen supplemented by minimal trilene or ether. Cyclopropane is also suitable. In cases of diabetes mellitus it is advisable to use some form of nerve-block which may be supplemented by a light gas and oxygen. When the mother is in poor condition, or there is foetal distress, the anæsthetist is faced with the same problem as occurs in a difficult forceps delivery under similar conditions: he must protect the mother from the shock of the obstetrical manœuvres; yet he must not depress the already enfeebled vital functions of the child. This is one of the chief reasons why some form of nerve-block has so many advocates.

Under general anæsthesia, should laryngeal spasm occur through the patient being too light, or for any other reason, the anæsthetist must devote his immediate attention to seeing that the patient is adequately oxygenated. Then, and not before, should he start to worry about the depth of anæsthesia. I believe it to be a beneficial practice to give the mother pure oxygen from the moment the delivery of the baby starts until the cord is clamped.

References

- Minnitt, R. J. (1947): "Gas and Air Analgesia," 3rd edition, London.
Tonn, G. R. (1946): *South. med. J.*, 39, 154.

THE CHOICE OF ANÆSTHETIC IN ELDERLY PATIENTS

By E. H. RINK, B.M., B.Ch., D.A.

Anæsthetist, Guy's Hospital.

WHEN faced with a wet and slippery road on a dark night, a first-class driver does not alter his technique in any essential way. He merely redoubles his normal safeguards and precautions; he avoids rapid acceleration and braking, but he reaches his destination very nearly as quickly and safely as he does under good conditions. It is very much the same thing in anæsthetizing bad-risk and especially old patients. All agents which are used on the fit may be administered to the aged, but nearly always in modified doses and rather slowly. Attention to such vital matters as the maintenance of a perfect airway and the avoidance of anoxia should be intensified, and the closest possible watch kept on the state of the circulation.

Anæsthesia for a necessary operation should never be withheld from a patient on the score of old age alone. It must be remembered that advanced age is only reached by those of sound constitution, and that, unless some special condition exists which renders it inadvisable, anæsthesia may be very well tolerated even by individuals in the nineties. Nevertheless, there are some special considerations to be borne in mind when dealing with such patients, and neglect of them will inevitably lead to disappointments and disasters.

GENERAL CONSIDERATIONS

As age advances, *the basal metabolic rate* tends to become lower; therefore less of all anæsthetic agents will be required to produce a given result than in the case of younger patients, and particular care must be taken not to overdose with such drugs as pentothal which are not excreted unchanged. Premedication should be very much modified; it is probably better to avoid hyoscine and scopolamine in patients over sixty-five or, if it is necessary to use them, to halve the normal dose. Morphine should also be used sparingly, and the best premedication for an old man about to undergo prostatectomy, for example, is probably morphine, $\frac{1}{4}$ of a grain (11 mgm.), with atropine $\frac{1}{100}$ of a grain (6.5 mgm.).

Old people stand *anoxia* very poorly; therefore anæsthetic mixtures in which the oxygen percentage is likely to be diminished should be avoided. This, translated into practical terms, means that nitrous oxide should be little used, the tendency being rather to give cyclopropane in a rich oxygen atmosphere, adding ether if it appears advisable. The maintenance of a perfect airway is essential in anæsthetizing any patient, but it is doubly important in the case of the elderly, and no means of ensuring it should be neglected. Old people also stand *blood loss* badly, and it is therefore im-

portant, in operations in which this is likely to be at all severe, to correct it as it occurs by means of an intravenous drip. It is easy, however, to overload the circulation in such cases, and thus the rate of the transfusion must be constantly controlled by observation of the blood pressure.

The respiratory system.—As age advances, there is a tendency, particularly in males, for the ribs to become relatively, occasionally totally, fixed, and for respiration to become predominantly diaphragmatic. There is also a marked tendency to chronic bronchial infection. This combination of circumstances makes postoperative chest complications extremely probable, especially after abdominal operations and repairs of hernia. They may best be minimized by the use of preoperative breathing exercises, and of such anæsthetic sequences as will ensure that the patient regains consciousness at the earliest possible moment after the operation. In order to obtain such a result after a long abdominal or thoracic operation, deep anæsthesia must at all costs be avoided, and the necessary relaxation provided either by nerve-blocking with local anæsthetics or by relaxant drugs such as curare. Spinal anæsthesia is poorly tolerated by the aged, and should be avoided. Always the lightest degree of anæsthesia which will produce the required result should be aimed at. The modern tendency of surgeons to get their patients moving and out of bed early after operations is a most important step in the prophylaxis of chest complications, and they are clearly abetted in this matter by rapid recovery from the anæsthetic.

The factor which does most to limit the success of surgery in the aged is, of course, the state of *the cardiovascular system*, and this should be carefully assessed by the anæsthetist, having particular regard to functional efficiency as shown by exercise tolerance. In this connexion more may be learned by a study of the patient's daily habits than by formal tests. Only the existence of actual heart failure at the time need absolutely contraindicate the administration of an anæsthetic, but myocardial insufficiency short of failure will obviously make for a poor prognosis, and should be pointed out by the anæsthetist. A patient suffering in this way should not die during the operation if he is carefully anæsthetized, but he is likely to do so within a few days of a severe operation. In such conditions it is for the surgeon, when he has been put in possession of the facts, to decide whether or not the risk is justified.

After these general considerations, it is now possible to discuss procedure in a more particular manner.

PREOPERATIVE PREPARATION

All patients probably benefit from a stay of a few days in hospital or nursing home before a severe operation, and this applies especially to the elderly. The time should be spent resting quietly, although not mainly in bed, and in familiarizing themselves with their new surroundings and attendants. The anæsthetist will do well to see his elderly patient as soon as possible, in

THE CHOICE OF ANÆSTHETIC IN ELDERLY PATIENTS

By E. H. RINK, B.M., B.Ch., D.A.

Anæsthetist, Guy's Hospital.

WHEN faced with a wet and slippery road on a dark night, a first-class driver does not alter his technique in any essential way. He merely redoubles his normal safeguards and precautions; he avoids rapid acceleration and braking, but he reaches his destination very nearly as quickly and safely as he does under good conditions. It is very much the same thing in anæsthetizing bad-risk and especially old patients. All agents which are used on the fit may be administered to the aged, but nearly always in modified doses and rather slowly. Attention to such vital matters as the maintenance of a perfect airway and the avoidance of anoxia should be intensified, and the closest possible watch kept on the state of the circulation.

Anæsthesia for a necessary operation should never be withheld from a patient on the score of old age alone. It must be remembered that advanced age is only reached by those of sound constitution, and that, unless some special condition exists which renders it inadvisable, anæsthesia may be very well tolerated even by individuals in the nineties. Nevertheless, there are some special considerations to be borne in mind when dealing with such patients, and neglect of them will inevitably lead to disappointments and disasters.

GENERAL CONSIDERATIONS

As age advances, *the basal metabolic rate* tends to become lower; therefore less of all anæsthetic agents will be required to produce a given result than in the case of younger patients, and particular care must be taken not to overdose with such drugs as pentothal which are not excreted unchanged. Premedication should be very much modified; it is probably better to avoid hyoscine and scopolamine in patients over sixty-five or, if it is necessary to use them, to halve the normal dose. Morphine should also be used sparingly, and the best premedication for an old man about to undergo prostatectomy, for example, is probably morphine, $\frac{1}{4}$ of a grain (11 mgm.), with atropine $\frac{1}{100}$ of a grain (6.5 mgm.).

Old people stand *anoxia* very poorly; therefore anæsthetic mixtures in which the oxygen percentage is likely to be diminished should be avoided. This, translated into practical terms, means that nitrous oxide should be little used, the tendency being rather to give cyclopropane in a rich oxygen atmosphere, adding ether if it appears advisable. The maintenance of a perfect airway is essential in anæsthetizing any patient, but it is doubly important in the case of the elderly, and no means of ensuring it should be neglected. Old people also stand *blood loss* badly, and it is therefore im-

that much smaller doses suffice for them than for younger patients, and that it may be very slowly destroyed. It is inadvisable therefore to use it continuously for a long anæsthesia, as prolonged narcosis will often result. It is, however, an ideal agent for the induction of anæsthesia, or for short and minor surgical procedures. Bromethol (*avertin*) should only be used in very restricted dosage as the metabolic rate is already low; it is probably best avoided in old people owing to its prolonged effect.

Nitrous oxide is harmless in itself but, as its use may easily be associated with some degree of suboxygenation, it is probably better not to use it in the elderly except for very short procedures, such as the extraction of teeth.

Chloroform should be avoided in view of its known harmful effects on the liver and heart, both of which are especially vulnerable in the patients under consideration. *Ether*, on the other hand, is far less harmful to them than is generally supposed. Provided that prolonged deep narcosis with it is avoided and that the airway is perfect, it has little irritant effect on the respiratory passages, and it produces no ill-effects on the circulatory system. Deep anæsthesia with ether produces a metabolic upset which may be very harmful but, with the alternative methods now available, this should never be necessary.

Cyclopropane is even more useful, on account of its ease of administration, of the extremely smooth induction which may be obtained with it, the high oxygen atmosphere in which it must be given, and the comparative rapidity of recovery from it. These properties make it theoretically ideal, but in practice it must be given with great care, as it may have an adverse effect on the heart. A pulse rate of under 60 to the minute is an indication to discontinue its administration, as is also the appearance of any cardiac irregularity; and as either of these phenomena may occur at a comparatively light level of anæsthesia, one must always be prepared to substitute ether for it. This will nearly always produce a return to a normal condition of the pulse, after which it is usually possible to resume with cyclopropane. It has been stated by some authorities, notably by Guedel, that bradycardia and cardiac irregularity may be safely ignored when they occur during cyclopropane anæsthesia. This may be true in the case of a healthy young adult, but it would be dangerous doctrine if applied to the old.

Trichlorethylene may be used as an adjuvant to nitrous oxide and oxygen, and is useful on account of its non-explosive properties, but the same cardiac phenomena may occur as with cyclopropane, and it should only be used to obtain light anæsthesia.

Curare is a most useful drug, producing, as it can, profound muscular relaxation in combination with light degrees of anæsthesia. For this reason it is especially valuable for elderly patients in whom, as has been seen, it is most important to avoid deep anæsthesia. In these cases it must be given with great care; and it must always be remembered that it will be destroyed in the body more slowly than will be the case in younger patients, and that

order to assess his state of health and to embark on any preoperative measures that appear necessary, such as breathing exercises or attention to the teeth, if any remain. These patients are often apprehensive, and it is a kindly and useful action to explain to them that their age is no bar to a successful operation. The surgeon has probably told them this already, but they will be pleased to have the reassurance repeated. Sleep is important to them, and should be secured by drugs if necessary. Old people are often anxious about the action of their bowels; they usually have some favourite purgative, and they should be allowed to continue taking it. Violent purgation before an operation is unnecessary and harmful. Whatever their habits with regard to alcohol and tobacco, these must be accepted as almost immutable; great harm may be done by unwise and usually futile efforts to enforce sudden abstinence from either.

Preoperative starvation also, should be avoided, and the object should be to bring the patient to the theatre in a good state of nutrition. Old people are apt to have touchy digestions, and apprehension will do nothing to help this; therefore liberal quantities of glucose should be given during the previous twenty-four hours. The last meal should be given four hours before the time of operation, and the last drink two hours later.

Premedication should, as stated above, be very moderate in amount; respiratory depression is easily produced in old people, and can be very harmful. It should also be remembered that sedative drugs often have an unduly prolonged action and should not be lightly repeated. Hyoscine often produces uncontrollable excitement in the elderly, and should if possible be avoided. It is as a rule only desirable to use it in cases in which it is intended to employ controlled respiration, that is, in thoracic operations; before these it is advisable to give only half the customary dose, $1/300$ of a grain (0.23 mgm.).

THE ANÆSTHETIC

In all the problems of anæsthesia it will be found that the skill of the anæsthetist and his careful methods are of more importance than are the actual agent or agents to be used. It will therefore not be out of place to emphasize once again that the most important factor making for success in anæsthetizing unfit or elderly patients is scrupulous care in administration. Anæsthesia must be induced slowly, anything in the way of spectacular methods eschewed, and a perfect airway must be meticulously maintained by whatever means are called for in a particular case. A liberal excess of oxygen should also be given. Anæsthesia should be maintained at the lightest level which will suffice for the operation which is being performed, and a rapid recovery must always be aimed at; an anæsthetic which looks and appears perfect at the time may still kill an old patient if it is too deep, and if prolonged unconsciousness and depression result from it.

Pentothal is well tolerated by the aged, provided that it is remembered

the closure of the peritoneum, it is better temporarily to deepen the general anæsthesia than to add further curare, which would then still be acting when the patient was returning to bed. As soon as the peritoneum is closed, all anæsthesia should be stopped and oxygen given; reflexes should then have returned and the patient be moving by the time that he reaches his bed.

THORACIC OPERATIONS

Up to a comparatively short time ago, major thoracic surgery was considered to be contraindicated in elderly subjects. More recently, however, with the great advances which have been made both in surgical technique and in anæsthesia, a bolder line has been taken, and this section is written from a personal experience of several lung resections in patients over sixty years of age, and of three resections of the œsophagus and stomach, two of them successful, in patients over seventy. The dangers of thoracic surgery are naturally greater in old patients than in young ones, but, as in other branches of surgery, age in itself should not be considered as a bar to the performance of a necessary operation, and it would without doubt be wrong not to attempt to remove an operable carcinoma of the lung or œsophagus simply because a patient is elderly. Apart from the ever-present risk of circulatory failure, the greatest danger is caused by postoperative retention of purulent bronchial secretions; this may best be countered by careful bronchoscopic aspiration at the end of the operation, which should be followed by a rapid return to consciousness, and by a rigorous system of breathing exercises and postural coughing. Blood replacement is most important during these severe operations; it is usually necessary to give about three pints of blood during a pneumonectomy, and often nearly four during a gastro-œsophagectomy. Needless to say, the rate of transfusion must be regulated by frequent observations of the blood pressure. Old people do not stand an open pneumothorax well unless controlled respiration is carried out; this may best be attained with light cyclopropane anæsthesia, assisted by curare, and given by means of a large cuffed endotracheal tube. Very careful preoperative assessment and preparation, with special attention to nutrition, to breathing exercises, and to the correction of anæmia by transfusion, are called for in these cases.

CONCLUSION

Few other operations carry the same special risks as those on the thorax and abdomen, and nothing need be said about the anæsthetic requirements for them, except to emphasize again the general principles which have already been stressed. It is true of all anæsthesia, but most especially of the anæsthesia of old people, that the things that matter most are not the drugs to be used but the skill, care and experience with which they are given, and with which the case as a whole is handled.

therefore the administration should be so planned that it will not be necessary to give any supplementary dose near to the end of the operation. The best and safest plan is to establish a light degree of anæsthesia and to give the curare intravenously just before the start of the operation; it is better to start with a small dose and add to it if necessary than to give the whole estimated dose at once. Naturally, the anæsthetist must be prepared to undertake artificial pulmonary ventilation or to assist respiration at any moment, as even a quite short period of hypoxia may be fatal to an old person. These difficulties must be faced; it is quite wrong to withhold the benefits of curare from old people on account of them. The dangers associated with its use may be more striking, but they are less grave than those of prolonged deep anæsthesia.

Muscular relaxation for abdominal surgery may also be obtained by *field- or nerve-blocking* with local anæsthetics. The total quantity to be injected must be strictly limited in old people, who should probably not receive more than 1 gm. of procaine, or corresponding doses of other local anæsthetic drugs. To achieve a sufficiently widespread effect while keeping within these limits very dilute solutions should be used. It must be remembered that the vitality of the tissues decreases with age, and that necrosis may occur from their overdistension or from the use of excessive quantities of adrenaline added to the local anæsthetic solution.

High *spinal anæsthesia* should not be used in elderly patients as their power of adaptation to vasomotor changes is likely to be limited. Low spinal anæsthesia is not open to this objection, but it is still better avoided in old people, because they will not tolerate well the postoperative period of immobility in a flat position which is necessitated by it.

ABDOMINAL OPERATIONS

Apart from the frequency of the operation of prostatectomy in old men, extensive and severe operations for intra-abdominal neoplasms are sometimes called for. The lines on which anæsthesia for these operations should be planned have already been indicated; after light premedication, anæsthesia should be induced with a minimal dose of pentothal and continued with cyclopropane or ether, as indicated in the particular case. With operations on the upper abdomen especially, it is often helpful to have a small tube in the trachea under the anæsthetic mask; this will ensure a perfect airway while the anæsthetist is injecting curare or attending to the intravenous drip, which should always be available during severe abdominal operations, and it will also make it possible to use light anæsthesia without the risk of laryngeal spasm when the surgeon is handling sensitive viscera. As has already been said, relaxation should be obtained either by means of curare or one of its substitutes, or else of local anæsthesia; never by deep anæsthesia. If, however, the relaxation from curare seems to be wearing off just before

sibility of a diffuse and chronic osteomyelitis which may destroy large parts of the jaw, if teeth and mandibular bone fragments have not received full attention. The most serious complication of upper jaw fractures concerns the entry of infection to the meninges through dural tears overlying associated fractures in the floor of the anterior cranial fossa. In addition, there have to be considered the chronic infections of the antra and other sinuses, and the chronic dilatation and infection of the lachrymal sac which so often follows traumatic obstruction of the naso-lachrymal duct. Diplopia, which is seen in unreduced malo-maxillary fractures when the ball of the orbit is depressed, may sometimes recover spontaneously, but this is not certain unless the bony parts are reduced.

EARLY TREATMENT

The major threats to life in facial accidents are suffocation and then, much more rarely, hæmorrhage and meningitis.

(1) *Preservation of airway*

The risk of death from suffocation in a facial injury is highest in the unconscious patient. However extensive the injury the vast majority of conscious patients will themselves find the position in which they can most comfortably breathe and maintain adequate respiration. They should be allowed to do so and not be forced into any arbitrary posture. The unconscious patient is a different problem. He may be unconscious from associated head injuries or drunkenness. Relatively minor degrees of obstruction to the glottis may be sufficient to cause death. A small clot in the larynx descending from an associated fracture of the base of the skull may produce this result, or a bruised and swollen tongue may do the same thing, as may also inhaled vomit. Patients in whom the nasal airway is blocked by nasal fractures and clot are particularly prone to death from suffocation while still unconscious. It is most dangerous for any unconscious patient with a facial injury to be allowed to lie flat on his back. Tongue, clot, saliva or vomit, are all most liable to cause a fatal obstruction when the patient is supine.

Transport.—The patient must lie so that the tongue falls forward and saliva and clot run out of the mouth and nasopharynx and not down on to the larynx. He may therefore be transported in the prone position. In this event care must be taken to see that he does not suffocate by burying his head in the pillow. Many soldiers so transported during the recent war arrived at the end of their journey with the pillows stuck to the face with coagulated clot and saliva. Probably the best position for transport on a stretcher is the "renal operation" position. The patient is transported on his side, semi-prone; the under leg is flexed at the hip and knee to stabilize him, and the head lies in the crook of the underarm. Whichever of these two positions of transport is adopted, the unconscious patient with facial injury, and above all those who are bleeding into the nose or mouth, must have continuous supervision from roadside to hospital. The attendant medical man must be prepared constantly to pull the tongue forward and to mop out clot and saliva from the mouth and pharynx.

Suffocation during anaesthesia.—The dangers here are in the induction

FACIAL INJURIES IN ROAD ACCIDENTS

By PATRICK CLARKSON, M.B., B.S., F.R.C.S.

Casualty Surgeon, Guy's Hospital; Plastic Surgeon, Ministry of Health Plastic Centre, Basingstoke; Associate Plastic Surgeon, Royal Northern Hospital.

THE range of accidents which have to be considered extends from simple falls from bicycles on to gravel pathways to collisions in cars travelling at speed on concrete highways. In terms of tissue damage the range of injury is equally wide; but even the smallest degree of force applied to the face may cause a lasting disfigurement with a permanent sense of handicap to the patient, and indeed in many instances with permanent economic effects. The common lesion, small in terms of tissue damage but capable of causing considerable disfigurement, is the grey staining and tattooing produced by gravel and dirt ingrained in the dermis. At the other end of the scale, following major violence to the face, there may be complete disorganization of the facial skeleton and loss of whole features. These injuries can threaten life immediately by suffocation, and their full repair may be a prolonged affair of many stages, taking two to three years before the treatment is complete.

The injuries within the face which may follow either its impact at great force on to a dashboard or windscreen, or the sheering compression between a heavy wheel and road, are often multiple. A dozen to twenty separate facial fractures are not uncommon in a single serious case. When the upper jaw is affected there are especially likely to be associated fractures of the air sinuses, and tears in the dura may overlie these. The soft tissue injuries may include, as well as any obvious external lacerations and losses of whole features, sublingual hæmatomas which can threaten an acute obstruction to the glottis, or lacerations of the palate or buccal mucosa with a similar risk. Injuries to special soft tissue structures, such as the nasolachrymal ducts, the parotid and its ducts, the 7th nerve and the contents of the orbit, may complete the picture.

It is well to remember that the late complications of complex facial injuries are by no means limited to disfigurement. Serious derangement of function follows lack of full treatment to a major facial injury. These disabilities include, on the dental side, degrees of malocclusion which may be so great that the fitting of a denture is impossible, and the patient is therefore confined to a soft diet for life. Unreduced maxillary and mandibular fragments can produce this result. Scarring within the temporo-mandibular joint, or in the soft tissues around it, may so limit the excursion of the joint that the patient can only separate upper and lower incisors by a few millimetres. It may be impossible to fit a patient with a denture if the buccal sulcus has been obliterated by soft tissue damage and not restored by epithelial inlay. Added to these derangements of mastication is the pos-

by hæmatoma during transit to hospital. Hæmorrhage at the primary operation for an injury of the face and jaws can almost invariably be controlled by a local approach through the wound: proximal external carotid ligation is rarely necessary.

(3) *Cerebrospinal rhinorrhœa and dural tears*

Recognition of the rhinorrhœa may be extremely difficult. Many patients with it do not show clear fluid running out of the nostril on being sat up and tilted forward. In such patients it is the nature of the injury which indicates the presence of a complication, plus the presence of anosmia. Any high maxillary fracture following head-on injuries across the face and nose is liable to have associated fractures on the frontal and ethmoid sinuses which communicate through tears in the overlying dura with meninges and brain. Good stereoscopic X-rays may be necessary for recognition of the fractures in the ethmoid or frontal sinus walls. Such cases may show displaced bone fragments in the floor of the anterior cranial fossa, fissures through the upper sinus walls, and/or opaque air sinuses. Together with anosmia, these X-ray appearances may be taken as presumptive evidence of a dural tear. The treatment of this condition is the neurosurgeon's province.

TECHNICAL POINTS IN PRIMARY FACIAL REPAIR

Compound fractures of the jaw differs from compound fractures of other light bones only by the presence of teeth and the communication with the buccal cavity. One of the primary objectives of treatment is to exclude the buccal cavity by closure of the mucosa or, failing that, to prevent serious infection by prophylactic drainage. When involved teeth are removed and the mouth has been excluded, the course of a mandibular fracture is similar to that of fractures of comparably built bones elsewhere in the body. Injuries here have the added advantage that because the whole of most facial wound tracks is available for a complete excision, and facial tissues are highly vascular, and because remaining teeth generally provide a rigid fixation, soft tissue healing in the face tends to be rapid and quiet, provided primary treatment has been thorough. This primary phase of treatment is followed by an intermediate phase during which bony union occurs. The late phase is concerned with reparative surgery of the bone and soft tissues and is for the most part, outside the scope of this article.

Anæsthetic.—A great number of facial lacerations caused by vehicle accidents can be, and are, best treated under local anæsthesia. This includes certain cases with jaw fractures, but on the whole most of the major bony injuries are best treated under general anæsthesia. For this jaw and face work the endotracheal tube is indispensable. A cardinal feature of the anæsthetic is the pharyngeal toilet which follows the insertion of the tube, and its removal.

Toilet of soft tissues: removal of dirt stains and tattoo marks.—A most essential feature of the treatment of all facial lacerations is a thorough toilet

phase and in the postoperative period when the patient is returned to the ward. Deaths which could have been avoided had proper precautions been observed have been all too frequent.

During induction by pentothal a spasm of the glottis or the inhalation of a clot may cause a total arrest of respiration. It is therefore essential that this induction be done by anæsthetists familiar with the technique of rapid intratracheal intubation. If such anæsthetists are not available the surgeon is well advised to stand by during this phase prepared to do a "crash tracheotomy". Alternatively, the whole operation should be done under a local anæsthetic.

The danger in the postoperative period can be equally great. These accidental postoperative deaths most often occur in patients whose jaws are lashed together, who return to dark wards, or wards without nurses experienced in their care. The risk of suffocation is particularly high when there has been a nasal injury associated with a jaw fracture for which the jaws have been wired together, so closing off the buccal airway, at least in part. All patients with jaw injuries, if they leave the theatre unconscious, should go back to well-lit wards and have the full-time attention of a nurse until they have fully recovered consciousness. They must never be allowed to lie flat on their backs.

A short circuit of the airway is necessary for some jaw fractures. In cases of respiratory obstruction of the greatest emergency, in the field or at the roadside, laryngotomy is probably best because it is quickest, safest and easiest. In almost all other cases a high tracheotomy should be done. A high tracheotomy, with the tube inserted through an ellipse cut in the 2nd and 3rd tracheal rings, is chosen because a short circuit is seldom needed for jaw fractures for more than three to seven days. The special danger of a low tracheotomy is the possibility of erosion of a high division of the innominate. Briefly the indications for a tracheotomy in jaw injuries are as follows:—(1) When the jaws are wired together (inter-maxillary fixation) and the nasal airway is blocked; (2) when the facial injury is associated with injury of the pharynx or larynx; (3) whenever the surgeon is in real doubt about the adequacy of the airway or about the standard of attention which it is possible to provide postoperatively. It is always better to do too many rather than too few tracheotomies.

(2) *Arrest of hæmorrhage*

Even major neck vessels are very likely to show spontaneous temporary arrest. It is therefore seldom necessary at roadside or field to do more than apply an external dressing. Continued major primary arterial bleeding can be arrested by the application (while the carotid is occluded by digital pressure lower in the neck) of a hæmostat to the bleeding point. The hæmostat is left in position during transport to hospital. Alternatively, the hæmorrhage may be stopped by closure of the external wound by temporary skin sutures. If this second method is adopted, special care, that is, laryngotomy or tracheotomy, may be needed to prevent obstruction of the larynx

by hæmatoma during transit to hospital. Hæmorrhage at the primary operation for an injury of the face and jaws can almost invariably be controlled by a local approach through the wound: proximal external carotid ligation is rarely necessary.

(3) *Cerebrospinal rhinorrhœa and dural tears*

Recognition of the rhinorrhœa may be extremely difficult. Many patients with it do not show clear fluid running out of the nostril on being sat up and tilted forward. In such patients it is the nature of the injury which indicates the presence of a complication, plus the presence of anosmia. Any high maxillary fracture following head-on injuries across the face and nose is liable to have associated fractures on the frontal and ethmoid sinuses which communicate through tears in the overlying dura with meninges and brain. Good stereoscopic X-rays may be necessary for recognition of the fractures in the ethmoid or frontal sinus walls. Such cases may show displaced bone fragments in the floor of the anterior cranial fossa, fissures through the upper sinus walls, and/or opaque air sinuses. Together with anosmia, these X-ray appearances may be taken as presumptive evidence of a dural tear. The treatment of this condition is the neurosurgeon's province.

TECHNICAL POINTS IN PRIMARY FACIAL REPAIR

Compound fractures of the jaw differs from compound fractures of other light bones only by the presence of teeth and the communication with the buccal cavity. One of the primary objectives of treatment is to exclude the buccal cavity by closure of the mucosa or, failing that, to prevent serious infection by prophylactic drainage. When involved teeth are removed and the mouth has been excluded, the course of a mandibular fracture is similar to that of fractures of comparably built bones elsewhere in the body. Injuries here have the added advantage that because the whole of most facial wound tracks is available for a complete excision, and facial tissues are highly vascular, and because remaining teeth generally provide a rigid fixation, soft tissue healing in the face tends to be rapid and quiet, provided primary treatment has been thorough. This primary phase of treatment is followed by an intermediate phase during which bony union occurs. The late phase is concerned with reparative surgery of the bone and soft tissues and is for the most part, outside the scope of this article.

Anæsthetic.—A great number of facial lacerations caused by vehicle accidents can be, and are, best treated under local anæsthesia. This includes certain cases with jaw fractures, but on the whole most of the major bony injuries are best treated under general anæsthesia. For this jaw and face work the endotracheal tube is indispensable. A cardinal feature of the anæsthetic is the pharyngeal toilet which follows the insertion of the tube, and its removal.

Toilet of soft tissues: removal of dirt stains and tattoo marks.—A most essential feature of the treatment of all facial lacerations is a thorough toilet

phase and in the postoperative period when the patient is returned to the ward. Deaths which could have been avoided had proper precautions been observed have been all too frequent.

During induction by pentothal a spasm of the glottis or the inhalation of a clot may cause a total arrest of respiration. It is therefore essential that this induction be done by anæsthetists familiar with the technique of rapid intratracheal intubation. If such anæsthetists are not available the surgeon is well advised to stand by during this phase prepared to do a "crash tracheotomy". Alternatively, the whole operation should be done under a local anæsthetic.

The danger in the postoperative period can be equally great. These accidental postoperative deaths most often occur in patients whose jaws are lashed together, who return to dark wards, or wards without nurses experienced in their care. The risk of suffocation is particularly high when there has been a nasal injury associated with a jaw fracture for which the jaws have been wired together, so closing off the buccal airway, at least in part. All patients with jaw injuries, if they leave the theatre unconscious, should go back to well-lit wards and have the full-time attention of a nurse until they have fully recovered consciousness. They must never be allowed to lie flat on their backs.

A short circuit of the airway is necessary for some jaw fractures. In cases of respiratory obstruction of the greatest emergency, in the field or at the roadside, laryngotomy is probably best because it is quickest, safest and easiest. In almost all other cases a high tracheotomy should be done. A high tracheotomy, with the tube inserted through an ellipse cut in the 2nd and 3rd tracheal rings, is chosen because a short circuit is seldom needed for jaw fractures for more than three to seven days. The special danger of a low tracheotomy is the possibility of erosion of a high division of the innominate. Briefly the indications for a tracheotomy in jaw injuries are as follows:—(1) When the jaws are wired together (inter-maxillary fixation) and the nasal airway is blocked; (2) when the facial injury is associated with injury of the pharynx or larynx; (3) whenever the surgeon is in real doubt about the adequacy of the airway or about the standard of attention which it is possible to provide postoperatively. It is always better to do too many rather than too few tracheotomies.

(2) *Arrest of hæmorrhage*

Even major neck vessels are very likely to show spontaneous temporary arrest. It is therefore seldom necessary at roadside or field to do more than apply an external dressing. Continued major primary arterial bleeding can be arrested by the application (while the carotid is occluded by digital pressure lower in the neck) of a hæmostat to the bleeding point. The hæmostat is left in position during transport to hospital. Alternatively, the hæmorrhage may be stopped by closure of the external wound by temporary skin sutures. If this second method is adopted, special care, that is, laryngotomy or tracheotomy, may be needed to prevent obstruction of the larynx



(a)



(b)



(c)



(d)

FIG. 1.—PRIMARY TOILET AND REPAIR OF COMPOUND FRACTURES OF BOTH JAWS

These pictures illustrate the quick, quiet healing to be expected even in combined compound fractures of mandible and antrum, when treated by thorough toilet, minimal excision, watertight exclusion of mouth by mucosal flaps, removal of teeth, firm fixation, and primary closure. The sutures were out on the third day; there was union of the comminuted mandibular fracture by the third month. A picture over a year later (d).

with soap and warm water or, better still, with 1 per cent. cetavlon. The especial need for a most meticulous and thorough toilet with sponge, scrubbing brush, and fine forceps, is in abrasions and excoriations following falls on to roadways. Many of these will not show the ingrained dirt obviously at the primary stage: it will be obscured by clot and œdema; but if this dirt is left in the tissues, and it is chiefly in the dermis, it will produce a permanent disfigurement consisting of a grey streaky tatoo. The toilet should occupy five to ten minutes in every case: when excoriation and abrasion is a feature the time allowed for it should be much longer. Figure 1 is an example—admittedly a special case—of ingrainment of mud in a mine wound. In this case the soap and water, scrubbing brush, and fine forceps toilet took over twenty minutes. The primary operation is often the only occasion at which all dirt and pigment can be removed, short of major late excisions needing repair by free grafts and flaps.

Soft tissue lacerations.—Vehicle accidents of the face do not often cause major loss of soft tissue. The common pictures are:—superficial excoriations and abrasions; deep and bevelled cuts of cheeks and lips by glass; full-thickness, irregular lacerations of the lips surrounded by considerable bruising; and, occasionally, massive semi-avulsed flaps comprising part or whole of cheeks, lips and nose. The great majority of these wounds can be repaired by approximation. The basis of treatment is skin-edge excision, undermining, and closure in layers using multiple sutures of fine material. A minority of cases in which soft tissue has been completely avulsed need closure after marginal excision by a local flap or free graft. Relatively small losses in special regions—alar margins, eyelids—can sometimes only be repaired by a primary graft or flap. Most primary flaps and free grafts need a later revision.

It is my belief that even straight, unabraded, clean cuts are best treated by a minimal marginal excision. The reason for this is that only the knife will ensure the non-bevelled edge which can alone be approximated with complete accuracy, and produce the object of treatment—a uniform, flat, hairline, supple scar of the same colour as the surrounding skin. Furthermore, the most rapid and quiet healing, that is, healing in two to four days, is not consistently seen throughout the whole extent of the wound unless there has been marginal excision of the skin edges. Without this uniform quick healing, sutures must be left in longer and will cause additional permanent marking.

This marginal skin excision may be done with a no. 15 blade, the wound being held tense by hooks at the extremities. When the wound is irregular a useful manœuvre is to pass first a no. 15 blade round its margins under the skin, thus mobilizing a small skin flap of 2 to 4 mm. in depth. This mobilized skin edge is fixed by light hæmostats and is then readily excised to give a non-bevelled edge, using $4\frac{1}{2}$ in. straight, sharp, pointed scissors.

To prevent late depressions appearing in the scar it is essential that a layer of fat be accurately apposed under the sutured skin edge. For this reason most facial lacerations are best further undermined after skin-edge excision. This undermining must be uniform, and must leave a fatty layer which can be approximated



(a)



(b)



(c)



(d)

FIG. 1.—PRIMARY TOILET AND REPAIR OF COMPOUND FRACTURES OF BOTH JAWS

These pictures illustrate the quick, quiet healing to be expected even in combined compound fractures of mandible and antrum, when treated by thorough toilet, minimal excision, watertight exclusion of mouth by mucosal flaps, removal of teeth, firm fixation, and primary closure. The sutures were out on the third day; there was union of the comminuted mandibular fracture by the third month. A picture over a year later (d).

(a)



(b)



FIG. 2.—LATE CORRECTION OF INGRAINED FACIAL DIRT

(1) BY SANDPAPER ABRASION.—(a) Shows the late effects on a child's face of compression on a road by the metal wheel of a dray. These pictures illustrate the limitations rather than the advantages of the method of sandpaper abrasion. When the dirt is diffusely in dermis and epidermis it can be removed by abrasion with sandpaper, which was done here with improvement (b). The deeper linear streaks in the subcutaneous tissues need serial excision.



FIG. 3.—LATE CORRECTION OF INGRAINED DIRT IN FACE

(2) BY SERIAL EXCISIONS AND WOLFE GRAFT.—The opportunity to remove these streaks of ingrained dirt by scrubbing at primary toilet was missed. Much of the dirt is in the subcutaneous tissue and the case is not suitable for sandpaper abrasion only. It was treated by serial excisions and, in the chin region, by a Wolfe graft plus irradiation (by Mr. Carter Braine). Photos with close focus and without makeup.

(a)

(b)

(c)



FIG 4—MALUNION OF EDENTULOUS JAW FRACTURE TREATED BY REFRACTURE AND PIN FIXATION

This series shows the use of extra-oral pins as a means of jaw fixation when teeth are missing. There was gross malunion of a right horizontal ramus fracture. This was treated by refracture reduction and pin fixation, (c) shows his condition six weeks later and after correction of the chin scar.

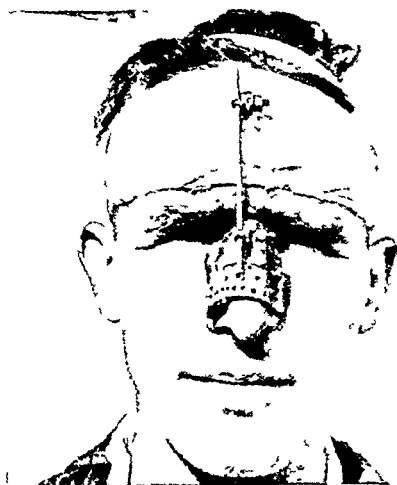


FIG 5—PRIMARY FIXATION OF UNSTABLE NASAL FRACTURE

This patient had had five previous nasal fractures which always united with a displacement to the right. The present reduction was very unstable and led to the adoption of this type of primary fixation by an appliance to P.O.P. headcap. This elaborate splint is seldom necessary.

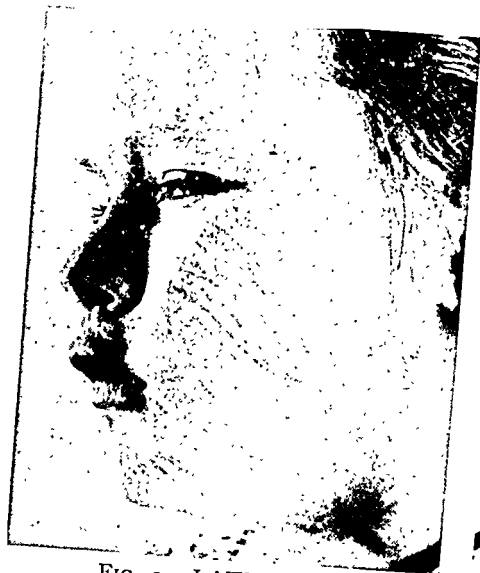


FIG. 2.—LATE CORRECTION OF INGRAINED FACIAL DIRT
(1) BY SANDPAPER ABRASION.—(a) Shows the late effects on a child's face of compression on a road by the metal wheel of a dray. These pictures illustrate the limitations rather than the advantages of the method of sandpaper abrasion. When the dirt is diffusely in dermis and epidermis it can be removed by abrasion with sandpaper, which was done here with improvement (b). The deeper linear streaks in the subcutaneous tissues need serial excision.



FIG. 3.—LATE CORRECTION OF INGRAINED DIRT IN FACE
BY SERIAL EXCISIONS AND WOLFE GRAFT.—The opportunity to remove these streaks ingrained dirt by scrubbing at primary toilet was missed. Much of the dirt is in the subcutaneous tissue and the case is not suitable for sandpaper abrasion only. It was treated by serial excisions and, in the chin region, by a Wolfe graft plus irradiation (by Mr. Carter). Photos with close focus and without makeup.

deep to the skin sutures, as well as facilitating skin closure without tension. In the face it is safe to undermine for 2 to 5 cm., and often more. The surgeon must be prepared, before undertaking this step, to pay special care to the hæmostasis; spurting bleeders are best ligated, others may be twisted off. In the deeper layers devitalized tags and grossly soiled layers of muscle are removed with scissors, which are conveniently used, too, for marginal excision of mucosa. These deeper layers are adequately closed by interrupted fine 000 or 0000 catgut on atraumatic needles.

There is a variety of suture material available for the skin closure. When interrupted sutures are used, and they are the most generally useful type of suture in facial lacerations, thin (04-06) serum-proof suture silk (deknetel) is probably best. It is soft, ties a snug and stable knot in two loops, and causes very little reaction. Nylon and plastosutes may be used; but their knots are less secure and are more bulky. The interrupted sutures are inserted at about 3-4 mm. intervals, enclosing bites of about 3-4 mm. of skin edge. Inversion of skin edges is checked by inserting the needle with the holder held by the hand in full pronation, and by the use of Gillies' skin hooks to hold the edge everted while the needle is inserted. When the laceration is straight, a continuous subcuticular suture with stainless steel wire, gauge 40, is best; its insertion needs practice. As Wallace has pointed out, tantalum wire is easier to handle than S.S. wire and for this reason is preferable, when obtainable.

Special structures.—Soft tissue injuries of the face involving such structures as the facial nerve and the parotid gland deserve a separate note. Injury to the main trunk of the facial nerve, or to its main terminal branches near their origin, occurs sometimes when glass or metal fragments cause a compound fracture of the ascending ramus. A careful search should be made at primary operation for the filaments; they should be gently apposed by fine sutures of black silk. There is a reasonable prospect of considerable regeneration if this is done properly. If the nerve has to be re-explored later, the black sutures are a guide to the lesion.

Most lacerations of the parotid gland are of little consequence provided care is taken to close the overlying subcutaneous tissues and skin in layers. The majority of parotid fistulæ following facial lacerations may be expected to dry up spontaneously in three to six weeks.

Lacerations involving the main parotid duct are capable of primary repair; the divided ends are secured and anastomosed over a fine hollow cannula, using the finest suture material. Alternatively the proximal end of the duct may be implanted afresh into the buccal mucosa in front of the masseter, if this is practicable.

TREATMENT OF THE BONE FRAGMENTS

Fixation of jaw fragments.—The primary operative treatment of a jaw injury is a combined operation by dentist and surgeon, and the choice of dental fixation will depend chiefly upon the condition of the teeth.

Whatever the method of fixation of bone fragments, the upper and lower jaws are best fixed together (inter-maxillary fixation) at the completion of operation. In those maxillary fractures in which the maxillæ are "floating" and loose from their attachments to the base of the skull, the jaws (after I.M.F.) have to be supported by metal connexions to a plaster headcap to correct the tendency to downward displacement. It must be emphasized that the most rapid and quiet healing of the facial soft tissues can only be expected when there is rigid immobilization of the bony fragments.

Care of comminuted bone fragments and of teeth.—All except completely detached or grossly soiled mandibular fragments should be conserved at

(a)

(b)

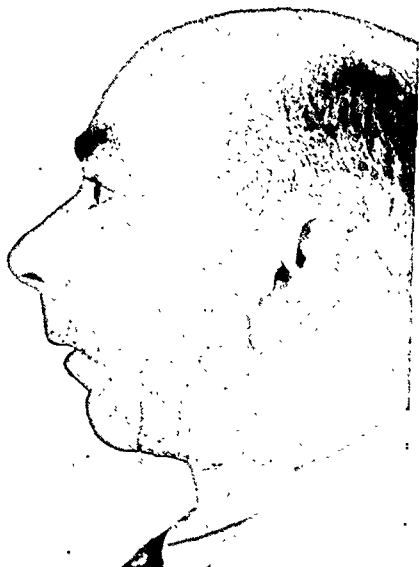


FIG. 6.—RELIEF OF BONY ANKYLOSIS OF TEMPOROMANDIBULAR JOINTS BY ASCENDING RAMUS RESECTION

This case of bony ankylosis—such as can follow infection of open condylar fractures—had had both condyles removed with only transient relief 20 years before. A false joint was therefore made in each ascending ramus. Three months later he wears at night the gag shown, and maintains his range of jaw movement. In (a) the edentulous gums are rigidly fixed at about 1 cm. apart; in (b) he has a range of movement of 2 cm. in the symphysis region.



FIG. 7.—LATE CORRECTION OF NASAL FRACTURES

Relatively minor injuries to the nose in childhood can, if not reduced, result in gross deformities in adult life—as in this case. It is sometimes wise when reducing such an old nasal fracture to remodel the skeletal structures completely and produce a nose more suitable to the face than the original.

the soft tissue wound during healing—two to four days in favourable cases. Oral hygiene and feeding must be considered together. The rule is that at the earliest possible date the patient is trained to do both these offices for himself, and is made to understand fully the necessity of spending several minutes after each meal syringing his mouth and polishing his teeth. The care of inter-maxillary fixation is a matter for close daily dental care throughout the period of union, if the reduction is not to slip due to broken wires, and union be delayed or faulty.

The soft tissue wound.—It is a prime requisite of facial sutures that they be removed before they cause permanent marking. Complete lack of suture marks can only be expected if they are taken out between the second and third days. But the facial wound will not have sufficient tensile strength to permit this early removal, unless it is a wound with freshly cut, non-bevelled edges. Wounds which have had such full primary treatment may have most of their sutures removed between twenty-four and forty-eight hours after operation; one or two sutures should be left for removal on the third day. The most generally satisfactory dressing, at operation and during the period of healing, is by tulle gras over penicillin-sulphathiazole powder.

When excoriations and abrasions with ingrained mud have been scrubbed, the same dressing is used; it is not disturbed for six to eight days, and is kept in place with a crêpe pressure bandage over gauze swabs.

The jaw fracture.—This intermediate period of healing concerns also the union of the fracture. Because of their proneness to infection from the mouth, from involved tooth sockets, and from devitalized comminuted bone fragments, delay in union has often been seen in jaw fractures. It is of high importance in the management of jaw fractures that the doctor should have clearly in his mind the rate of union to be expected in an uncomplicated case. Most linear fractures will show firm clinical union in three to six weeks. In all other fractures there should be clear evidence of union developing and increasing between the sixth and tenth weeks. When on testing the degree of union present, between the sixth and tenth week, there is lack of evidence of progress towards union, the cause should be sought. Involved infected teeth, or sequestra, or foreign bodies, are removed. Four weeks after healing of the soft tissue wound such fractures which still show inadequate progress to union should be treated by insertion of iliac medullary bone into the freshened fracture site. Union may be expected within four weeks of the grafting operation.

LATE REPAIRS

This article is not concerned with the late repairs of destroyed or displaced soft tissues, but a note may be made on the time at which facial scars should be revised and corrected. The sound general rule is to wait until all œdema, pinkness, and tenderness have gone from the scar. This may be in a month or six weeks; but it is more commonly of the order of six months. Penicillin certainly gives an additional margin of safety which was absent before.

primary operation. This means that in jaw fractures caused by vehicle accidents (as contrasted to those caused by missile wounds) mandibular fragments are seldom removed at primary operation. With the maxilla the situation is somewhat different. Conservatism is the rule concerning alveolar fragments and all fragments forming part of the orbital floor. In those rare and serious crash injuries in which the antrum is lashed widely open and its walls comminuted, it is wise to be relatively radical in removal of the comminuted fragments which lie in the wall of the antrum; that is, the same rules hold regarding vehicle accident injuries as for missile wounds of these bones, but only when there is gross comminution. Conservation of comminuted antrum fragments is commonly followed by antral disease and extensive late sequestration.

Teeth which are involved in the fracture line are best removed at primary operation. Exceptions to this rule are firmly impacted molar teeth, the extraction of which might cause considerable trauma to the fracture site, and single teeth on what would be edentulous posterior fragments if they were extracted. Such teeth which are left at primary operation to provide a temporary fixation may have to be removed later when the bone fragments are adherent by callus; if left in the fracture line indefinitely a low-grade infection may develop round them and delay union.

Drainage.—When a tooth involved in the fracture line has been left to provide fixation, or when there is doubt about the viability of comminuted bone fragments which have been left, or when there has not been a watertight closure of the buccal mucosa over the fracture site, external drainage, by corrugated rubber drain, should be provided for three to four days.

Fixation of malar fractures.—Of fractures of the facial skeleton other than the jaws, malar fractures need a special note. The displacement, with diplopia, which is seen in fractures of these bones is complex. The body of the bone is commonly displaced backwards and downwards and is tilted about a horizontal axis; it may, too, be rotated round a vertical axis. Many such malar fractures can be reduced by an elevator passed through the temporal fossa, and the reduction so obtained may be stable. When, however, the reduction is unstable, it is necessary to wire the malar to the external angular process.

Reduction and fixation of nasal fractures.—The disimpaction, manipulation and reduction of nasal fragments is best done by Walsham's forceps.

The septum is reduced and "ironed out" by flat Ash's forceps. The most satisfactory fixation is by a 3-4 in. x 2 in. plaster of Paris splint which extends down from the centre of the forehead across the glabella to lie across and fix either nasal bone. The nasal airway is maintained by small-calibre greased rubber tubes passed into the nasopharynx. These need constant attention to prevent blockage by clot and mucus. Grossly comminuted and depressed fractures of the nasal bridge line commonly need a late restoration by a bone graft.

CARE DURING THE INTERMEDIATE OR HEALING PHASE OF JAW FRACTURES

The early concerns of the patient are food, oral hygiene and the dressing of

teeth may be corrected by grinding or extraction of molars. There is, however, no doubt that many of the gross malocclusions seen are best treated by complete remobilization of the fracture by open operation on the mandibular or maxillary fracture site (fig. 4).

Trismus.—Trismus is best treated prophylactically with active exercises from the earliest date that intermaxillary fixation is released. Chewing gum is always useful; a wedge for passive dilatation may be needed for obstinate cases. Those cases in which there has been involvement of the temporomandibular joint followed by ankylosis may not respond to conservative treatment (fig. 6). Nor are they likely to respond to mechanical exercises or dilators applied to cast metal splints on the teeth—methods which are often successful in the relief of trismus due to soft tissue scarring.

For these cases of ankylosis either the head and neck of the condyle must be removed—and this operation is often best done by a post-auricular approach—or an Esmarch type pseudo-arthritis in the ascending ramus can be made. In this last operation a wedge of the ascending ramus above the angle and a half to one inch in vertical depth is excised on one or both sides. The teeth are fixed by a gag in the maximum opening position of the bite and held there for a fortnight. Subsequently the gag is worn at nights for a period of six to eight weeks. Cast metal splints applied to the teeth and fitted with flanges guiding the bite during the daytime into its proper occlusion may be necessary. The operation is technically simpler than the removal of the condylar head and, with full dental cooperation, the late results are more uniformly satisfactory.

Late nasal and facial contour restorations.—Gross asymmetry and disfigurements of the face are common in unreduced maxillary fractures. If the occlusion is reasonable, refracture may not be indicated. Much of the disfigurement and asymmetry may be masked by the insertion, into the cheeks and over appropriate parts of the jaws, of either soft materials such as dermo-lipomatous grafts, or of more rigid contour restoration material, such as cartilage (preserved cadaver, or ox cartilage), autogenous bone, or polythene moulds. Tantalum is on the whole unsuitable for use in the face. In superficial sites it is subject to temperature changes and tends to be extruded (fig. 4 and 7).

The late correction of an unreduced nasal deformity is more complicated. The nasal bones must be remobilized completely by saw and chisel from maxillary, frontal, and septal attachments. The alæ are completely mobilized from the skin, thinned and remodelled as necessary, and replaced into the symmetrical position. Considerable remodelling of alæ and nasal tip may be necessary if the fracture has occurred and been uncorrected in youth. Relatively minor nasal fractures, if left uncorrected during the period of growth, can cause considerable late disfigurement and asymmetry (fig. 7). The best end-results in a nasal fracture with gross depression of the bridge-line may only be obtained by insertion of a bone or cartilage graft along the bridge line, generally after mobilization and reduction of nasal bones and alæ. Of the two types of graft, bone and cartilage, bone gives the more certain long-term result. It is impossible to guarantee that distortion or absorption will not occur in grafts of cartilage.

The correction of minor degrees of septal deflection may be done at the same time, and indeed is part of the nasal reduction. Major deflections of the septum are the concern of the E.N.T. surgeon and, in most cases, are best treated three months before the nasal reduction.

But even with penicillin an œdematous or pink skin edge cannot be undermined with safety—and undermining is an integral part of all late scar revisions.

Late removal of ingrained dirt.—A most valuable and important technique for the removal of the ugly staining produced by ingrained dirt in the facial skin has recently been introduced here from the U.S.A., where it was first used. In this technique (fig. 2) the affected area is rubbed with sandpaper (gauge 00) to remove epidermis and the superficial layers of dermis in which most of the dirt is lying. After systematic and thorough rubbing with sandpaper—a process which may take ten minutes or over an hour depending upon the area—a dressing of tulle gras and a pressure bandage are applied. Dirt which is deeper than the dermis is generally present as discreet lines or points and can be excised later (fig. 2 and 3).

LATE OPERATIONS ON THE FACIAL SKELETON

The treatment of delayed union in mandibular fragments by medullary chip grafting has been indicated. Certain other complications of fractures of the facial skeleton need discussion. They are:—the diplopia, the dacryocystitis and epiphora due to blockage of the naso-lachrymal duct, malocclusion, trismus, and the late nasal reductions.

Diplopia.—The diplopia which is seen in some malo-maxillary fractures may sometimes disappear spontaneously without reduction of the fracture. This relief takes place over a period of six to twelve months by accommodation of the ocular muscles. It is too uncertain and too slow a process to be accepted; the malar fracture should be reduced and if necessary fixed by wiring to the external angular process at primary operation. If seen late in malunion, refracture by open operation may be necessary.

In some cases in which there has been a depression of the middle and medial parts of the orbital floor, malar reduction alone may not be enough to correct the diplopia; the orbital floor must be elevated by strips of either cartilage or bone. In my experience packing of the antrum seldom gives permanent relief of the diplopia to this difficult minority group of malar fractures. There remains, too, a residual group not relieved by any surgical procedure on the facial skeleton. Their relief is a matter of selective tenotomy of the extrinsic ocular muscles by the ophthalmic surgeon.

Dacryocyst-rhinostomy.—A chronic distension and infection of the lachrymal sac with constant epiphora is one of the more common and most troublesome late sequelæ of maxillary fractures which have caused obstruction to the naso-lachrymal duct. When examination shows that the duct is firmly blocked with a dilated palpable sac from which muco-pus can be expressed, a dacryocyst-rhinostomy is indicated. In this operation a new and more direct channel is made from the sac horizontally into the upper nasal cavity. It is essential that the new channel be lined with mucosal flaps.

Malocclusion.—Trismus and malocclusion are late complications of maxillary and mandibular fractures. Minor degrees of malocclusion of the

although for inducing sleep soluble barbitone, 5 grains (0.32 gm.) or more, is usually better. In cases liable to need a stronger sedative I prefer *seconal sodium*.

PENICILLIN AND THE SULPHONAMIDES

For infections, penicillin should certainly be available. In most cases, in contradistinction to urban and hospital practice, one daily injection of 100,000 or 200,000 units will usually give satisfactory results. Of the sulphonamides I think sulphamezathine is the most generally useful as no special dietary precautions are necessary, and its side-effects are so slight that it can be taken by patients who are ambulant or working. Children also tolerate it well. For septic skin conditions, such as impetigo, I have found nothing to equal an extremely fine suspension of sulphathiazole ("mikraform" sulphathiazole) and it is fortunately usually successful in the difficult and dangerous skin infections of early infancy.

SOME EMERGENCIES

Remedies for *cardiovascular emergencies* are all too few. Morphine is essential for coronary thrombosis. I have not found any marked benefit from nicotinic acid either in coronary or cerebral thrombosis, although fairly large doses of potassium citrate combined with caffeine do some good in the latter condition, even though the pharmacological basis for the use of potassium citrate is almost certainly wrong. For the acutely failing heart nothing equals cardiazol-ephedrine, which is also most valuable in asphyxia neonatorum, but it is only for emergency use until digitalis, caffeine, aminophylline or other requisite drug has begun to take effect. Capsules of amyl nitrite are needed for angina pectoris and tablets of trinitrin for slower but more persistent action. It is curious how many patients with hypertension feel more comfortable with a stomach mixture of the bismuth type, and not a few actually show some reduction of the blood pressure after a time.

Although bismuth is now officially discounted for *dyspeptic conditions* it is, in practice, most valuable in *appendicular dyspepsia*, in which magnesium trisilicate usually fails entirely to relieve symptoms. If to such a mixture (bismuth carbonate, 10 to 15 grains [0.65 to 1.0 gm.], magnesium carbonate, sufficient to regulate the bowels, and equal parts of peppermint water and chloroform water) is added about 60 minims (3.5 c.cm.) of takadiastase solution, these patients will often be able to enjoy a reasonably full diet without restrictions and vow that they can obtain better medicine in the country than they got in the towns (where pharmacological incompatibilities are perhaps more regarded). Incidentally, dyspeptic patients often do not do well on tonics but improve on a bismuth mixture long after they ought to be able to do without it. When an acid tonic can be tolerated I find that the outmoded strychnine and acid phosphate mixture often gives better results than the mixture with hydrochloric acid. It is perhaps worth mentioning that practitioners often fail to get benefit from these mixtures because they use such small doses of strychnine solution. Thera-

DRUGS IN COUNTRY PRACTICE

By W. N. LEAK, M.D.

IN writing this short article I have decided not to make it a purely formal list of drugs and their uses, but rather to indulge in a ramble round the therapeutic countryside, which may perhaps be more suitable to the rural aspects of medicine. The drugs chosen should be those which have a wide application rather than being the ideal for any particular condition. Whilst this article deals mainly with emergency drugs, I have added a few notes on less urgent conditions, the fruit of 33 years' practice, which may be of help to those practising in rural areas.

DRUGS FOR THE RELIEF OF PAIN

Pain is the most common affection requiring urgent treatment and it should certainly be relieved unless this will cloud a diagnosis, for pain by itself may jeopardize recovery, whilst the patient who begins to feel better a few minutes after his doctor has seen him will be rightly gratified. *Morphine*, hypodermically, or in many conditions *morphine*, *hyoscine* and *atropine*, is most generally useful for severe pain, although *pethidine* HCl (100 mgm.) can often be used with benefit instead, especially in obstetric work and when pain is due to smooth muscle spasm. By the mouth, *pethidine* tablets (25 mgm.), repeated as necessary, are usually much better than *morphine*, unless it is wished to check a diarrhœa, and they are one of the few pain-relieving drugs which can usefully be taken when the patient has been vomiting or has acute indigestion. Otherwise compound *codeine* tablets (B.P.) are satisfactory in milder cases of pain, but when there is myalgia or headache in febrile illnesses the old *compound aspirin tablet* (N.H.I.—*aspirin* 6 grains [0.4 gm.], *phenacetin* 2½ grains [0.16 gm.], *Dover's powder* 2 grains [0.13 gm.]) has not been equalled by more modern introductions for relieving aches and reducing temperature. Its mild constipating action is also helpful in many of the diarrhœic conditions which are rather common at present. Finally, I would commend *compound phenacetin tablets* (B.P.) for the patients who cannot take *aspirin* or who have indigestion. These tablets are also most useful for infants and children; a quarter of a tablet every four hours for each year of age is often a godsend for febrile or painful conditions in these little patients.

This leads me to say that *syrup of chloral* is a valuable addition to most medicines for children who have to be kept in bed. It not only makes things much easier for their parents, but by preventing restlessness it conserves the patients' strength and avoids many complications caused by throwing off the bedclothes and so getting chilled. For small patients the practitioner should also carry tablets of *phenobarbitone soluble*, ¼ grain (16 mgm.), which can safely be given to a child of one year. They are useful as an occasional sedative, whilst being of particular benefit in convulsive conditions. Larger tablets, 1 grain (65 mgm.), are, of course, useful for adults,

PRURITUS IN INDUSTRY

By A. V. MAGEE, M.B., CH.B.

Works Medical Officer, Dyestuffs Division, Imperial Chemical Industries Ltd., Manchester.

"AN Itch is worse than a Smart" says the proverb and the patient usually says it is worse than pain. Nevertheless, itching is a valuable sign to the physician and the scratch that accompanies it brings blood and nourishment (and often sepsis) to the diseased part. In industry not all cases of itching are due to the work being done by the patient, and the following few examples are cases in point:—

(a) Four workers in a chemical laboratory complained of generalized itching. The appropriate treatment cured them of scabies in twenty-four hours.

(b) Two workers handling rats developed an intolerable itch associated with large wheals. Some of the rats had been bred in an infested bedroom, sold to a dealer, and carried human bugs to the workers.

(c) A worker handling dermatitic substances complained of a widespread rash with some itching. A "herald spot" indicated the diagnosis.

(d) Another worker developed a very severe itch with œdema of the face, hands, feet, scrotum and throat. A meat-pie—not from the works' canteen—was the cause.

(e) A chemist had a severe itching and a vesicular rash affecting the fingers and palms. The attack was fairly acute and strongly suggested a works' condition, but several attacks had occurred in previous summers and his pompholyx disappeared when he deserted his potting shed and shunned artificial manure.

(f) A young woman presented a widespread erythematous rash which she claimed was due to her work in a shed containing chemical substances. She described the itch as severe, laid off work and supported her claim for compensation with medical certificates. It was noted, however, that the tongue was inflamed and fissured and her voice was decidedly husky. A few judicious inquiries in her home town led to a sample of blood being obtained and the Wassermann reaction was strongly positive. The itch in this case was, no doubt, of a "compensatory" nature.

In a factory, especially a chemical factory, the itching patient must claim the Medical Officer's close attention, for industrial dermatitis often starts with an itch accompanied, or preceded, by a very slight vesicular or erythematous rash on or between the fingers, on the face or neck, or any part exposed to the offending substance, be it solid, liquid or gaseous.

Recently the National Insurance (Industrial Injuries) Act, 1946, has come into operation and the employer is no longer liable to pay his dermatitic worker compensation. The case is dealt with by the Local Insurance Officer who communicates with the employer to satisfy himself that the worker has, in fact, contracted dermatitis in the course of his employment. "Injury benefit" is then payable for 156 days from the date of development of the disease. Should the claimant still be unfit for work after that period of time, he comes before a Medical Board which decides whether the dermatitis has resulted in (a) a loss of faculty; (b) whether the loss of faculty is likely to be permanent; (c) at what degree the extent of disablement resulting from a loss of faculty is to be assessed, and what period is to be taken into account by the assessment.

peutic nihilism is usually the result of therapeutic timidity, and it must be remembered that most formularies inevitably have doses on the small side so as not to upset the sensitive patient, often so small as to be unable to give the effect which a more accurate dosage for each patient would produce.

Every rural practitioner's bag should contain one or two glycerin suppositories—the children's size will suit most patients. Also, a few morphine and ipecacuanha lozenges for irritating cough. Insulin, of course, should be at hand for diabetic emergencies.

Obstetric emergencies may need treatment. I have already mentioned pain-relieving drugs for labour, cardiazol-ephedrine for asphyxia, sulphonamide and sulphathiazole for sepsis, so there remain the essential ergometrine and pituitrin for hypodermic injection, and pituitrin reminds me that adrenaline should be available for dealing with *asthma* and other *allergic phenomena*. Ephedrine or, better still, proprietary preparations such as "asmadyn" or "taumasthman" will often check a bad attack of asthma without the careful watching required for adrenaline, and without the danger of shock that it very occasionally produces. Adrenaline is also sometimes useful in dealing with hæmorrhage from a tooth socket or for adding to a local anæsthetic. For dealing with hæmorrhage in the newborn a vitamin K analogue, e.g. "kapilon", should always be at hand as an emergency treatment.

Anæsthesia.—Often in rural practice wounds have to be stitched, and injection round the wound edges of a local anæsthetic (novocaine is probably best) makes the process vastly easier both for patient and doctor. A surface anæsthetic is needed for the removal of foreign bodies from the eye. A solution of amethocaine (anethaine) has the advantages that it does not dry the cornea nor affect the pupil or accommodation. One of the modern imitations of the original sedonan is valuable for otitis media, but use of these drops requires more rather than less care and vigilance in rural practice. Indeed this caution applies to many of the remedies mentioned because, just on account of their efficiency, they can mislead the unwary with serious consequences, especially in the country where supervision is difficult.

CONCLUSION

The face—and the pace—of rural medicine is constantly changing. My father always said that a catheter was the most useful thing he carried. My grandfather, who always rode on horseback, never left dental forceps out of his saddlebag. To-day I seldom use either. The countryman is naturally conservative but shrewd. It is better to use few drugs and know them thoroughly than to rush after every novelty. Only so can one acquire knowledge by which to appraise the value of new introductions. Those I have mentioned have been tested on many occasions and they can be trusted to do their job. With ingenuity I can pack them, and many others, into a 12" attache case, together with hypodermic and serum syringes, ophthalmoscope, auroscope and Tycos sphygmomanometer. This case I carry everywhere, and with it most emergencies can be met.

TOBIAS AND THE DOCTORS

By W. K. CONNELL, M.B., F.R.C.S.

WHILST it is true that many physicians, and a few surgeons, have written with power, charm and impeccable style, few of them have achieved an international reputation in *both* medicine and creative literature. The immortality of Dr. John Brown rests entirely on his beautiful and moving essays, equalled only by those of Charles Lamb. Rabelais lived in an age when medicine was little more than witchcraft, and neither he nor Sir Thomas Browne did much to raise it to a higher plane. Maugham and Linklater took but a hasty glance at medicine and then forsook it. Conan Doyle tried hard to make a living in general practice, and Sherlock Holmes was one happy consequence of his failure. It is true that medicine always meant a great deal to O. H. Mavor ("James Bridie") who practised with success both as general practitioner and as consultant. The case of Cronin is somewhat different. Here is a man who could have been a great physician, but who became instead the author of some highly popular novels.

The truth is that Medicine and Creative Art are exacting mistresses, neither of whom will tolerate a rival. Oliver Wendell Holmes perhaps came closer than any other to a dual conquest, for he adorned his anatomical chair, lectured brilliantly, contributed to medico-legal knowledge, wrote a valuable paper on puerperal sepsis and coined the immortal word, "anæsthesia". Yet when his name is mentioned, it is to recall the haunting beauty of the "Chambered Nautilus" or "The Last Leaf", or the delicious humour and humanity of "The Autocrat of the Breakfast Table".

EARLY DAYS

At about the middle of the eighteenth century two Scotsmen, born within easy reach of Glasgow, descended upon London and proceeded to make history. Neither owned much beyond the clothes that covered him and the genius that inspired him; yet one became the father of scientific surgery and pathology, whilst the other exercised an influence only second to that of Fielding on the development of the English novel. These men had certain qualities in common. Both were exceptionally observant; their courage was dauntless, their resolution inflexible, their capacity for hard work infinite. But in most other respects they were poles apart. Their social backgrounds differed; for whereas John Hunter was a son of the soil, Tobias George Smollett came of a wealthy and distinguished family with roots traceable to the fifteenth century. One of Smollett's forbears had actually blown up a ship of the Spanish Armada. Tobias was proud of this ancestry, but it put no money in his pocket because his father, having sinned past forgiveness by marrying the woman of his choice, had been virtually disinherited. Yet Tobias owed much to his pedigree, for adventure

A claimant who has developed a permanent idiosyncrasy to chemicals may present the Board with a pretty problem, for at the time he appears before the Board his skin may be clear; but a few minutes after returning to work he may be itching from head to foot. "Patch testing" might be suggested by the Board, but this is far from satisfactory and in the end it will be for the works' Medical Officer to point out to the employee and employer that a complete change of occupation is indicated and dismissal of the worker justifiable.

PATHOLOGY OF PRURITUS

So little is known of the pathology of itching that it is sufficient to say here that itching becomes pathological at an unknown level and that the sensitiveness of the skin varies within wide limits and depends largely upon the patient's psychological make-up.

TREATMENT

If the itch is due to the worker's occupation he should be removed from its environment immediately, regardless of all other considerations, including the wishes of the patient or the management. Until the patient is cured, or the itch proved not to be occupational, he should remain away from all work except perhaps in the fresh air on an outdoor job. Neglect of this precaution may allow just enough time for him to become sensitized for life.

The affected parts may be dressed with a simple application such as boracic ointment and protected from the patient's nails. Emulsion of benzyl benzoate diluted with water relieves the itch. If the pruritus reaches intolerable heights, an injection of "allergosil" gives great relief in thirty minutes. We have found that 3 or 4 antistin tablets daily will often relieve the itch in chemical dermatitis, but the results have been such that we can only recommend this type of drug as worth a trial. In three cases of fungoid infection, antistin had no effect on the itch.

SUMMARY

A few cases of common skin diseases have been mentioned as occurring in a chemical factory to show the importance of a correct diagnosis, not only for the patient's welfare but to protect the employer from bogus compensation claims. Antihistamine and other drugs have been mentioned, not as cures for all industrial dermatitis cases, but as a means of relieving the itch. It might be suggested here that some workers prone to industrial dermatitis are, in fact, histamine reactors.

Pruritus is an important and valuable aid to the works' Medical Officer in finding early dermatitis cases and allowing him to institute treatment, in many cases, before an idiosyncrasy is fully established and the worker's livelihood put in jeopardy.

virate stuck in the passage. While they remained thus wedged together, they descried two of their brethren posting towards the same goal, with all the speed that God had enabled them to exert; upon which they came to a parley, and agreed to stand by one another."

They then took possession of the patient's antechamber, and shut the door, "while the rest of the tribe posted themselves on the outside as they arrived; so that the whole passage was filled, from the top of the staircase to the street-door. . . . The three leaders of this learned gang had no sooner made their lodgement good, than they began to consult about the patient's malady, which every one of them pretended to have considered with great care and assiduity. The first who gave his opinion said the distemper was an obstinate arthritis; the second affirmed that it was not other than a confirmed pox; and the third swore it was an inveterate scurvy. This diversity of opinions was supported by a variety of quotations from medical authors, ancient as well as modern." In the end, the noise made by the faculty awakened the patient "from the first nap he had enjoyed in the space of ten whole days. . . . The colonel, seeing himself beset with such an assemblage of solemn visages and figures, which he had always considered with the utmost detestation and abhorrence, was incensed to a most inexpressible degree of indignation. . . . He sprung out of bed with incredible agility, and, seizing one of his crutches, applied it so effectually to one of the three, just as he stooped to examine the patient's water, that his tie-periwig dropped into the pot, while he himself fell motionless on the floor."

A truly despicable character is the naval surgeon, Dr. Mackshane, drawn from Smollett's personal adventures during the ill-fated expedition to Carthagen. This doctor was "grossly ignorant, and intolerably assuming, false, vindictive, and unforgiving; a merciless tyrant to his inferiors, an abject sycophant to those above him." This wretch, in order to curry favour with Captain Oakum, had all the ship's sick paraded on the quarter-deck, where he accused them of malingering and the captain sentenced them to various inhuman punishments, as the result of which the majority of them died. By these means the sick-list was reduced from sixty-one to less than a dozen. When, later, the ship came under heavy fire from the shore batteries of Boca Chica, Mackshane, "after having crossed himself, fell flat on the deck" and would have remained there for the duration of the battle had not the first mate plainly told him "that if he did not get up immediately and perform his duty, he would complain of his behaviour to the admiral, and make application for his warrant. This remonstrance effectually roused Mackshane, who was never deaf to an argument in which he thought his interest was concerned; he therefore rose up, and in order to strengthen his resolution, had recourse more than once to a case-bottle of rum. . . . Being thus supported, he went to work, and arms and legs were hewed down without mercy."

Outspoken comments on the handling of the Carthagen exploit appeared later in "The Critical Review" and aroused the anger of Admiral Knowles, who, refusing Smollett's prompt offer to give satisfaction on the field of honour, successfully prosecuted the author for libel.

A macabre blend of *syphilis* and sentiment characterizes one of the many strange adventures of Roderick Random, a young doctor whose fortunes fluctuated like the ups and downs of an ague chart. On this occasion his body had "become infected by a distemper contracted in the course of an amour", so that, impoverished and deserted by his friends, he was in a sorry state.

"I considered, however," says our hero, "in the intervals of my despondence, that I must in some shape suit my expense to my calamitous circumstances; and with that in view hired an apartment in a garret near St. Giles's, at the rate of ninepence per week. In this place I resolved to perform my own cure, having first pawned three shirts to purchase medicines and support for the occasion. . . . One day when I sat in this solitary retreat, musing upon the unhappiness of

was in his blood, he had an inborn passion for literature, and his manners had the subtle charm that goes with breeding. His general education had been as sound as Hunter's had been defective, for at Dumbarton Grammar School he had come under the influence of John Love, at once a great classical scholar and a great teacher. The results of this education were soon apparent. "The Regicide" may not be a first-class play, but it is surely a remarkable effort for a lad of eighteen.

Arrived at the metropolis, the paths of our two Scotsmen diverged. Hunter, single-minded and in no doubt concerning his ultimate goal, girded himself forthwith for a direct and brave assault on the mysteries of human and comparative anatomy. And here we shall leave him.

For Smollett the issue was by no means so clear, and for his journey there was no highroad but rather a perplexing maze of devious and difficult tracks through an uncharted jungle. In the words of David Herbert, he "began to look out for employment in the Army, in the Navy, as a doctor, as an author, or in any other gentlemanly way of toiling to the sweat of his brow or of his brain; but before and above all he wanted to see his tragedy on the stage of Drury Lane or Covent Garden". There being no takers for "The Regicide", he turned to medical practice, only to fail as dismally as Conan Doyle. But it would be a mistake to think of him as torn between two loves. He had but one love, medicine being for him merely a bread-study from which he vainly hoped to win a living and perhaps some social uplift. He seems indeed to have despised doctors almost as heartily as did Molière and Montaigne, and in his writings he never fails to present them as ludicrous or ignoble figures. Yet doctoring supplied him with much vivid local colour and, indirectly, by leading him to the high seas as assistant-surgeon to the "Cumberland", impelled him to the creation of "such sailors as have never existed, before or since, in the literature of any language".

EIGHTEENTH CENTURY MEDICINE

Smollett's opinion of the medical fraternity at Bath can be easily inferred from various passages in "Peregrine Pickle".

Peregrine "perceived that, among the secret agents of scandal, none were so busy as the physicians, a class of animals who live in this place, like so many ravens hovering about a carcass. . . This whole body fell under the displeasure of our hero who . . . concerted a stratagem, which was practised upon the faculty in this manner. Among those who frequented the Pump Room was an old officer, whose temper, naturally impatient, was, by repeated attacks of the gout, which had almost deprived him of the use of his limbs, sublimated into a remarkable degree of virulence and perverseness. He imputed the inveteracy of his distemper to the malpractice of a surgeon who had administered to him while he laboured under the consequences of an unfortunate amour; and this supposition had inspired him with an insurmountable antipathy to all the professors of the medical art. . . Peregrine, by means of Mr. Pipes, employed a country fellow, who had come to market, to run with great haste, early one morning, to the lodgings of all the doctors in town, and desire them to attend the colonel with all imaginable despatch. In consequence of this summons, the whole faculty put themselves in motion; and three of the foremost arriving at the same instant of time, far from complimenting one another with the door, each separately essayed to enter, and the whole trium-

of water, which he found in the room, in a basin; when he was interrupted by the prescriber, who advised him to use the contents of the chamber-pot, which, being impregnated with salt, would operate more effectually than pure element. Thus directed, the governor lifted up the vessel, which was replete with medicine, and with one turn of his hand discharged the whole healing inundation upon the ill-omened patient, who, waking in the utmost distraction of horror, yelled most hideously."

In the light of modern investigations into the crystalline forms of many viruses, Smollett's reference to "spiculated particles" is somewhat remarkable.

Among other medical diseases briefly dealt with by Smollett there are references to the treatment of confluent *smallpox* by means of whisky, and the use of buttermilk in *phthisis*. There is also a short description of the outbreak of "bilious fever" (undoubtedly yellow fever) which completed the discomfiture of the Carthage expedition. "Three-fourths of those whom it invaded died in a deplorable manner, the colour of their skin being, by the extreme putrefaction of the juices, changed into that of soot".

Like all true creative artists Smollett knew how to blend pathos with his humour, and it is impossible to read the ludicrous details of poor Mrs. Trunnion's phantom pregnancy without feeling a tug at the heart-strings.

The Trunnions are so splendidly alive that the reader lives with them, sharing their joys and sorrows, and sympathizing with the one-eyed commodore's ill-concealed vanity over "the promised harvest of his own sowing". The old salt was so misguided as to boast of his virility at the club, while his wife "in all her visits and parties seized every opportunity of declaring her present condition, observing that she was forbid by her physicians to taste such a pickle, and that such a dish was poison to a woman in her way; nay, where she was on a footing of familiarity, she affected to make wry faces, and complained that the young rogue began to be very unruly, writhing herself into divers contortions, as if she had been grievously incommoded by the metal of this future Trunnion." And so the story moves to its sad denouement. "They could not for ever remain under the influence of this sweet delusion, which at last faded away, and was succeeded by a paroxysm of shame and confusion, that kept the husband within doors for the space of a whole fortnight, and confined his lady to her bed for a series of weeks, during which she suffered all the anguish of the most intense mortification; yet even this was subdued by the lenient hand of time."

Throughout his works Smollett has plenty to say on the subject of *Public Health*, and, being an unusually observant and intelligent man, his remarks are very much to the point. He compares London unfavourably with the country in such matters as food, wine, and water; condemns white bread; criticizes the disposal of night-soil in Edinburgh; inveighs against the total absence of sanitation in Bath, and points out the serious danger of infection through drinking its polluted waters; emphasizes the urgent need for proper Health Regulations; and praises the beneficial effects of golf. Smollett may indeed well be considered one of the pioneers of preventive medicine.

Surgery (until John Hunter got properly under way) was in a very backward state in Smollett's time, and amputation, with its hideous mortality, was almost the routine treatment for any open fracture. Smollett (in the character of Roderick Random) supported a more humane conservatism,

my fate, I was alarmed by a groan that issued from a chamber contiguous to mine, into which I immediately ran, and found a woman stretched on a miserable truckle-bed, without any visible signs of life." He discovers that the patient is a young prostitute to whom he had recently paid court under the mistaken belief that she was a lady of quality. His chivalry and generosity of heart aroused, he revives her with "cinnamon water, a little mulled red wine and a toast", and then learns that the poor creature is dying from the combined effects of syphilis and hunger, a charlatan having fleeced her of all the money she had. He makes her share his apartment, thus saving expense, and immediately sets to work to cure both himself and the unfortunate girl, "finding in her not only an agreeable companion, whose conversation greatly alleviated my chagrin, but also a careful nurse. . . . Her condition filled me with sympathy and compassion; I revered her qualifications; looked upon her as unfortunate, not criminal, and attended her with such care and success that, in less than two months, her health, as well as my own, was perfectly re-established." All this, be it noted, happened long, long before the days of 606.

Of numerous references to *ascites* the most vivid is John Hatchway's letter describing the illness of Mrs. Trunnion.

"Cousin Pickle, [he writes] I hope you are in a better trim than your aunt, who hath been fast moored to her bed these seven weeks, by several feet of under-water lodging in her hold and hollop, whereby I doubt her planks are rotted so that she cannot choose but fall to pieces in a short time. I have done all in my power to keep her tight and easy, and free from sudden squalls that might overstrain her. And here have been the doctors, who have scuttled her lower deck, and let out six gallons of water. For my own part, I wonder how the devil it came there; for you know as how it was a liquor she never took in. But as for those fellows the doctors, they are like unskilful carpenters, that in mending one leak make a couple; and so she fills again apace."

Several allusions to hydrophobia reflect the terror inspired by that dread illness in eighteenth century Britain.

Thus, when Dr. Wagtail was bitten in the cheek by a harlot who had tried to blackmail him, he was left "in the utmost horror, not so much on account of the pain as the apprehension of the consequence of the bite; for by this time he was convinced of her being mad. Banter prescribed the actual cautery, and put the poker in the fire to be heated, in order to sear the place. The player was of opinion that Bragwell should scoop out the part affected with the point of his sword, but the painter prevented both of these dreadful operations by recommending a balsam he had in his pocket, which never failed to cure the bite of a mad dog. So saying he pulled out a small bladder of black paint, with which he instantly anointed not only the sore, but the greatest part of the patient's face, and left it in a frightful condition."

So much for the prophylaxis of rabies. Regarding treatment, there is the sad case of the painter, Pallet, whose dog-like howlings when soused with water were considered pathognomonic of hydrophobia. As soon as Pallet was asleep, a physician was brought to his bedside.

"The physician took notice of his breathing hard, and his mouth being open; and from these diagnostics declared that the *liquidum nervosum* was intimately affected, and the *saliva* impregnated with the spiculated particles of the *virus*, howsoever contracted. This sentence was still further confirmed by the state of his pulse, which, being full and slow, indicated an oppressed circulation, from a loss of elasticity in the propelling arteries. He proposed that he should immediately suffer a second aspersion of water, which would not only contribute to the cure, but also certify them beyond all possibility of doubt with regard to the state of the disease; for it would evidently appear, from the manner in which he would bear the application, whether or not his horror of water amounted to a confirmed hydrophobia. Mr. Jolter, in compliance with this proposal, began to empty a bottle

CURRENT THERAPEUTICS

XI.—THE MODERN TREATMENT OF EPILEPSY

By A. J. M. BUTTER, M.D.

Medical Officer, St. David's Hospital for Epileptics, Edmonton.

THE treatment of idiopathic epilepsy depends mainly upon the use of anticonvulsant drugs, but other measures to raise the physical and mental well-being of the patient may first be considered.

GENERAL MEASURES

Employment.—The usual rules of healthy living, often forgotten, need not be enumerated here but, in the case of the epileptic, the desirability of a regular routine, work, hobbies and physical exercise, requires emphasis. As regards occupation, the employable epileptic is to-day fortunate in being entitled to a certificate as a "disabled person" (obtainable from the rehabilitation officer at the local employment exchange) and, when this has been completed by a doctor, may be able to obtain suitable employment. The improvement in his general condition because of contentment in his work and the increased self-respect that it brings are often paralleled with a reduction in the number and severity of his fits. The electro-encephalogram has, within recent years, confirmed the impression of many observers that epileptic convulsions are less apt to occur when the mind is active and busy. For this reason, the child epileptic too, should, if at all possible, be kept occupied and not unnecessarily prohibited from attending school.

Various diets have been given extensive trials by different workers. Of these, only the *ketogenic diet* requires special mention. In intractable cases which do not respond well to drugs, the diet is well worth a trial, and this is especially true of child epileptics. In practice, however, even in an institution, it is found difficult to control because most adult patients subjected to it find it distasteful, are tempted to supplement their diet with forbidden foods, and finally state quite firmly that they would rather have their fits than the diet.

The same applies to treatment of epilepsy by *dehydration*, that is, the production of a negative fluid balance in the patient by reducing fluid intake to about one pint daily and administering diuretics, cathartics and diaphoretics. Advocates of this treatment have claimed a fair proportion of good results. Patients, however, are unwilling to persevere for long with the irksome restriction of liquid intake and one can feel some sympathy with their occasional surreptitious visits to the nearest source of drinking-water. Nevertheless, one part of this treatment is always worth remembering in any case of epilepsy, namely, the morning dose of salts, especially in patients who are taking bromides. This simple measure often results in a significant

and there is a good description of how he and Dr. Morgan saved the leg of Jack Rattlin whose tibia was broken by a fall from the main-yard. The ignorant Mackshane had recommended instant amputation, and agreed to withhold his hand only because he thought (and hoped) that his assistants would be discredited by the failure of *their* methods.

"Mr. Mackshane, flattering himself with the prospect of our miscarriage, went away, and left us to manage it as we should think proper. Accordingly, having sawed off part of the splinter that stuck through the skin, we reduced the fracture, dressed the wound, applied the eighteen-tailed bandage, and put the leg in a box, *secundum artem*. Everything succeeded according to our wish, and we had the satisfaction of not only preserving the poor fellow's leg, but likewise of rendering the doctor contemptible among the ship's company, who had all their eyes on us during the course of this cure, which was completed in six weeks."

How did an eighteenth century surgeon prepare for an operation? Smollett lets us into the secret in his description of an accident sustained by a certain squire Burdock.

The squire, involved in a public house quarrel, had had the worst of it in a bout at single-stick, and "the shame of this defeat had tied up his tongue," his silence being mistaken for coma due to a fracture of the cranium. It was decided that "there was a necessity for having him trepanned without loss of time", and a surgeon was summoned from York to perform the operation. He duly arrived "with his prentice and instruments." Having examined the patient's head, he began to prepare his dressings; though Grieve (a country apothecary from a neighbouring village) still retained his first opinion that there was no fracture, and was the more confirmed in it, as the squire had passed the night in profound sleep, uninterrupted by any catching or convulsion. The York surgeon said he could not tell whether there was a fracture until he should take off the scalp; but, at any rate, the operation might be of service, in giving vent to any blood that might be extravasated, either above or below the *dura mater*. The lady and her son were clear for trying the experiment; and Grieve was dismissed with some marks of contempt. . . . "Leaving the ladies in an apartment by themselves, we adjourned to the patient's chamber, where the dressings and instruments were displayed in order upon a pewter dish. The operator, laying aside his coat and periwig, equipped himself with a night-cap, apron, and sleeves, while his prentice and footman, seizing the squire's head, began to place it in a proper posture." But mark what followed! "The patient, bolting upright in the bed, collared each of these assistants with the grasp of Hercules, exclaiming in a bellowing tone, 'I ha'n't lived so long in Yorkshire to be trepanned by such vermin as you!' and leaping to the floor, put on his breeches quietly, to the astonishment of us all. The surgeon still insisted upon the operation, alleging it was now plain that the brain was injured, and desiring the servants to put him into bed again; but nobody would venture to execute his orders, or even to interpose when the squire turned him and his assistants out of doors, and threw his apparatus out at the window."

There would seem to be little doubt that Smollett possessed all the attributes of a great surgeon or physician, for he had wit, personal charm, shrewd Scottish common sense, a balanced mind, exceptional powers of observation and a profound knowledge of the medical science of his time. Why, then, did he fail in practice? The answer can only be that his first and true love was literature and that his heart never was in medicine—deeply though he had studied it. And this brings us back to our original thesis, namely that Medicine and Creative Art are exacting mistresses, neither of whom will tolerate a rival.

be kept, indicating whether they are major or minor and at what time of the day or night they occur. Concurrently, a record of the drug or drugs employed should be made.

Occasionally, a slight alteration in the treatment effects a dramatic improvement. To select a single example:—

A patient aged sixteen was for a time the storm-centre of St. David's Hospital (an epileptic colony), the ringleader in almost every mischievous enterprise, destructive, insolent, insubordinate and foul-mouthed. During eight months of consistent misbehaviour, he had 128 fits. Several drugs were tried without beneficial effect. When a suitable combination of drugs was, at last, discovered, his behaviour improved almost at once. During the following eight months only five fits occurred and he became obedient, reasonable, well-behaved and comparatively industrious.

Cases of this kind, which could be multiplied, encourage the perhaps illusory hope that, given time and observation, almost any case of epilepsy could be greatly benefited.

It may be convenient, in discussing the drug treatment of epileptics, to consider the various types of cases that are common. First of all, the patient who has very infrequent fits, say, about once a year or at even longer intervals, requires no special medicinal treatment at all and, in any event, will probably be unwilling to take medicine all the year round in order to prevent an occasional attack. Secondly, there is the type of patient whose fits are all nocturnal. As he is in bed he is not likely to fall and hurt himself. If, however, these nocturnal fits are severe and occur more often than once or twice a year, and especially if they are sometimes accompanied by biting the tongue and passing water, then the patient may be greatly benefited by phenobarbitone, one or two grains nightly. A third type of patient is he who has groups of fits, perhaps four or five occurring within forty-eight hours, at intervals of a few months. This type of man often knows himself, or it is obvious to those who are familiar with his peculiarities, that he is on the point of having a series of attacks. He may be irritable and depressed, or complain of giddiness, or uncomfortable abdominal sensations, or headache. When such warnings are manifested, then sodium bromide, three times a day in 20 grain (1.3 gm.) doses, plus phenobarbitone, also three times a day in 1 grain (65 mgm.) doses, may be successful in averting the series of fits or, at least, in preventing all but a mild attack. But probably most important of all is to give 3 grains (0.2 gm.) of calomel at night followed by 60 grains (4 gm.) of magnesium sulphate in the morning.

A more common case history is that the patient has three or four attacks of *grand mal* in a month all the year round and a large number of attacks of *petit mal*. In such a case, phenobarbitone, epanutin (soluble phenytoin), bromides, rutonal (phenylmethylmalonylurea) and other drugs may all be tried, alone or in combination and in various doses. In addition, tridione (3,5,5-trimethyloxazolidine-2,4-dione) may be helpful for the *petit mal*.

Phenobarbitone, used alone or in combination with other drugs, is still the most generally useful anticonvulsant. In a survey (Butter, 1945) of 375 cases of idiopathic epilepsy, observed in patients for periods ranging from six

reduction in the number of fits. Alcohol should be taken sparingly, if at all, for a single heavy dose of spirits may precipitate a fit, and heavy beer drinkers, whilst they may not become intoxicated, do "hydrate" themselves and so are predisposed to fits.

Electrical convulsion therapy, also, has its uses in epilepsy. Thus, in cases in which the patient's seizures are at fairly regular and therefore predictable intervals, an artificially induced convulsion may be desirable, and desired by the patient, since it can be arranged immediately before the expected attack as an "out-patient" treatment in the safety of a hospital bed instead of occurring without warning in front of a bus. In cases also in which there is an associated psychosis, improvement in the patient's mental condition may be obtained. Some workers maintain, in addition, that electrical convulsion therapy reduces the frequency of major attacks (Caplan, 1946).

Psychotherapy, in skilled hands, will, by resolving conflicts and raising morale, ameliorate the lot of a proportion of epileptics, but most psychiatrists would disclaim any special powers in influencing the incidence of the patient's convulsive seizures.

Surgical procedures are often valuable in cases of traumatic epilepsy and in convulsions due to intracranial tumours, but are not advocated in idiopathic epilepsy.

DRUG THERAPY

Although the treatment of idiopathic epilepsy by drugs is largely empirical, guidance may be obtained from a study of the familial and personal history of an individual epileptic, his peculiarities of physique and temperament, the nature and number and possible periodicity of his fits, and the time of day at which the fits ordinarily occur.

Fortunately, when an encephalogram (E.E.G.) is available the patient's particular type of epilepsy may be more accurately diagnosed and the most suitable drug, or drugs, thus selected for treatment (Symonds, 1948). The E.E.G. may confirm a diagnosis of true *grand mal*; or it may reveal that what appeared to be *petit mal* is, in fact, "minor *grand mal*". In both cases, phenobarbitone, alone or with epanutin, will probably be more appropriate than other drugs. Again, the E.E.G. may disclose a pattern of waves found in patients who suffer from so-called psychomotor attacks. Such patients have phases of mental confusion and disordered behaviour with or without convulsive movements. They are often difficult and dangerous patients and usually evoke less sympathy than perhaps they deserve. In their case, as a rule, epanutin produces the best response. Should the E.E.G. demonstrate true *petit mal*, then, in our present-day knowledge, the patient is not likely to respond to any other drug than tridione. Even with the help of the E.E.G., however, it may be found that observation over many months is necessary before the drug, or combination of drugs, is discovered which will best control the patient's fits and, at the same time, produce no marked toxic effect. A record of fits should therefore

of phenobarbitone and slightly more anticonvulsant. An alternative method of dealing with drowsiness due to phenobarbitone is to prescribe with it either benzedrine or methedrine.

In the very worst cases, when a patient may have hundreds of fits in a year and occasional status epilepticus, the following time-honoured mixture may prove to be most helpful:—

R Sodium bromide	10 grains (0.65 gm.)
Chloral hydrate	5 grains (0.32 gm.)
Tincture of belladonna	15 minims (0.9 c.cm.)
Chloroform water.....	to $\frac{1}{2}$ ounce (14.2 c.cm.)

This may safely be given twice or three times a day despite the high dosage of belladonna and, when required in severe cases, may be continued for months or years.

A change of drug, or combination of drugs, or increased dosage, may confer benefit for an indefinite length of time but, in a proportion of cases, adjustment of the dosage is found to be necessary at least once a year. In some cases, complete remission of fits does not prove to be an unqualified blessing and should perhaps not be aimed at, for disorders of conduct and, occasionally, an alarming excursion into status epilepticus may follow a long fit-free interval.

STATUS EPILEPTICUS

As to the treatment of status epilepticus, no single measure will invariably prove effective and, usually, several concurrent procedures are advisable. As the patient's condition precludes ordinary oral administration of his usual drugs, and as convulsions may continue for days, the hypodermic injection of 2 c.cm. of somnifaine or other equivalent for phenobarbitone, is obviously important. Somnifaine, a combination of two barbituric acid compounds, may be repeated at intervals of four hours. Also, a large dose of bromides and chloral hydrate may be given by means of a stomach-tube. Paraldehyde (21 c.cm. in 43 c.cm. of olive oil) may be given per rectum and repeated if necessary, but it is not always retained. Inhalations of chloroform may at least temporarily abate or abolish the convulsions and, if the patient is not too restless, lumbar puncture, with the withdrawal of a test tube full of cerebrospinal fluid, may prove to be beneficial.

TRIDIONE IN PETIT MAL

The treatment of the *petit mal* epilepsies was always disappointing until the introduction of tridione in America (Everett, 1944; Lennox, 1945, 1947; Richards, 1944). There is no doubt that this drug has a pronounced inhibitory effect on *petit mal* and offers new hope to those who have found other treatments unavailing. It is supplied in 0.3 gm. capsules, the dose being from two to six capsules daily. Because of its toxicity, however, it should be reserved for patients who suffer from frequent *petit mal* and are seriously inconvenienced by their disability. A few days after starting to

months to five years, it was found that phenobarbitone and epanutin were being used with good effect in the following number of cases:—

	Number of cases	Percentage of 375 cases
Phenobarbitone, used alone or in combination with other drugs	278	74.1
Epanutin, used alone or in combination with other drugs	85	22.6

Therefore for those patients who have several fits every month throughout the year, phenobarbitone will usually be found to offer the best line of attack. It may be given in doses of $1\frac{1}{2}$ grains (0.1 gm.) twice or thrice daily, gradually increased to 6 grains (0.4 gm.) or more daily. Should this produce little reduction in the number of fits, or cause drowsiness or other toxic symptoms, one capsule ($1\frac{1}{2}$ grains [0.1 gm.]) of epanutin may be added twice daily and cautiously increased to three, four, five or even six capsules daily.

The *dosage of epanutin* will be regulated according to the reduction of fits or the production of toxic symptoms such as pyrexia, skin rashes, hyperplasia of the gums, nausea, vomiting, tremulousness, intention tremor, ataxic gait, nystagmus, ptosis, slurring speech, insomnia, or mental confusion. Such toxic effects will mostly disappear within a few days after discontinuance of the epanutin and therefore it may be tried again, gradually, until the optimum non-toxic dose appears to be reached. The other drugs, such as bromide or phenobarbitone which the patient is taking, may gradually be reduced or withdrawn. There is a very narrow margin between the therapeutic and toxic dose. Two capsules of epanutin daily may be useless. Three daily may prove to be the perfect therapeutic dose, and four daily may produce pronounced toxic symptoms and signs in the same patient. In practice, it will usually be found that few patients can take more than three capsules ($4\frac{1}{2}$ grains [0.36 gm.]) daily without toxic reaction sooner or later. The average dosage of phenobarbitone is also about $4\frac{1}{2}$ grains (0.36 gm.) daily in the type of case under discussion. As epanutin is much less hypnotic than phenobarbitone, the two drugs may usefully be given together, and indeed this combination is one of the most satisfactory treatments of epilepsy to-day.

Mention must also be made of "mesantoin", not yet generally available in this country, but which appears to be a useful variant of epanutin, and "hydantal", which is a combination of mesantoin and phenobarbitone.

Rutonal or *prominal* may be given as an alternative to phenobarbitone, either alone or in combination with epanutin or other drugs. It is distinctly less soporific than phenobarbitone and can therefore make a welcome change for patients who complain of drowsiness. In almost all such cases, 3 grains (0.2 gm.) of rutonal will be found to be less hypnotic than $1\frac{1}{2}$ grains (0.1 gm.)

REVISION CORNER

THE USE AND ABUSE OF ASPIRIN

ASPIRIN is probably the most widely used drug at present on the market (2,296 tons were used in the U.S.A. in 1937); it is therefore important to bear in mind its pharmacological actions and toxic effects. Sensitivity to small doses is an occasional occurrence, variously reported as 1:1000 and 1:10,000, and may be alarming to patient and practitioner but is rarely fatal. A more precise knowledge of the fate and actions of aspirin in the body is of particular importance in view of the recent work on the treatment of rheumatic fever with massive doses of salicylates.

FATE OF ASPIRIN IN THE BODY

Gastroscopic study has shown that on coming into contact with the gastric mucosa, aspirin, either in tablet or powder form, causes a local irritation which may be intense enough to produce pin-point hæmorrhages, and even hæmatemesis has occurred, though rarely; this effect is much less noticeable with calcium aspirin.

Aspirin passes through the stomach, and a small proportion is absorbed from the bowel unchanged and exerts its well-known antipyretic and analgesic actions; the remainder is decomposed by the alkaline intestinal juices to acetate and salicylate. The latter is more slowly absorbed and exerts an analgesic effect which is about one-third to one-half that of aspirin. Sodium bicarbonate administered with aspirin speeds up the absorption and may lessen the tendency to gastric irritation, but it also hastens the excretion of the drug *via* the kidneys and its effect is therefore curtailed.

Approximately 60 per cent. of aspirin ingested is excreted in the urine as salicylic acid which reduces Fehling's solution and gives a positive test with ferric chloride—a bluish violet colour if present in large amounts (e.g. in attempted suicides) and a reddish-brown colour as with acetoacetic acid if present in smaller amounts. It is not uncommon for patients to bring their specimens of urine in aspirin bottles, and the discerning physician will exclude the presence of acetoacetic acid by finding a positive ferric chloride test persisting after boiling the urine.

When administered with alkalis such as sodium citrate, in which aspirin is soluble, decomposition occurs quickly, so the solution must be freshly made: 10 to 15 per cent. of the aspirin is dissociated in twenty-four hours and 100 per cent. in one week.

ACTIONS OF ASPIRIN

Aspirin has a non-specific analgesic effect and is used in a multitude of conditions, including migraine, arthritis, dysmenorrhœa, the neuralgias and the myalgias; doses varying from 10 to 30 grains (0.65 to 2 gm.) daily are usually adequate. Apart from its analgesic and antipyretic actions there are certain less well-known effects which may occur and which deserve emphasis:—

Sensitivity.—This is probably an example of drug allergy wherein the drug combines with a body protein to act as an antigen; antibodies then develop in the cells of many organs and further administration leads to a union of antigen and antibody with release of histamine. Sensitivity is more common with aspirin than with the other salicyl compounds and tends to occur in allergic individuals, although many of the latter can take aspirin with impunity. Oedema of the face and eyes, fever, skin eruptions, asthma and vasomotor rhinitis may occur; the urticarial elements respond well to antihistamine drugs such as anthisan and benadryl, and the asthma to adrenaline.

Emetic action.—Vomiting is a common occurrence when massive doses are given but may also occur with more moderate doses. This is probably largely due to central stimulation and in small part only to local gastric irritation.

take the drug, four patients out of five will probably report a reduction in the number of their *petit mal* attacks. A week or ten days later, about three-fourths of them may mention that on walking out of a building they find the light too bright. The phenomenon may be described as "dazzle", or "glare", or "a white mist over everything". Others may say that objects appear to have changed colour. In most cases, this disturbance of vision will not raise serious objections to taking the drug but, in a few instances, the patient will be glad to wear dark glasses to mitigate the effect. Some may be aware of slight drowsiness and others report hiccough, epigastric discomfort or unsteadiness in walking. The majority, however, will prefer to continue taking tridione, as the relief obtained from the reduction in their attacks more than outweighs the "dazzle phenomenon" or the other symptoms. Should a skin rash appear, discontinuance of the drug is advisable, but it may be introduced again in small doses when the condition has subsided.

In addition, there is one more toxic effect of tridione of which the patient will not be aware, except indirectly, and which calls for the utmost caution. In a high proportion of cases, blood counts reveal a reduction in the number of white blood corpuscles. Three fatal cases of agranulocytosis following the continued use of the drug have been reported in America. Therefore the supervision of all patients taking tridione must include monthly blood counts. Should the neutropenia be progressive, discontinuance of the drug is essential. Fortunately, in most cases, *petit mal* attacks remain absent or fewer in number for several weeks after the patient ceases to take tridione, and if a month or two later a satisfactory increase in the white blood count is reported the drug may again be cautiously introduced.

Finally, tridione is contraindicated in patients with severe renal or hepatic disease, in cases in which optic-nerve disease is already present, and in patients with a history of blood dyscrasia or of pronounced idiosyncrasy to drugs. Despite all this, the drug is a valuable one and much appreciated by the severely handicapped sufferer from *petit mal*. Doubtless, now that a start has been made, others of its type, but less toxic, will follow in the near future.

SUMMARY

Treatment in epilepsy is briefly considered under the headings of employment, diet, dehydration, electrical convulsion therapy, psychotherapy and surgery. Drugs, in particular phenobarbitone, epanutin and tridione, are discussed in some detail.

References

- Butter, A. J. M. (1945): *J. Neurol. Neurosurg. Psychiat.*, **8**, 49.
 Caplan, G. (1946): *J. ment. Sci.*, **92**, 784.
 Everett, G. M., and Richards, R. K. (1944): *J. Pharmacol.* **81**, 402.
 Lennox, W. G. (1945): *J. Amer. med. Ass.*, **129**, 1069; (1947) **134**, 138.
 Richards, R. K., and Everett, G. M. (1944): *Fed. Proc.*, **3**, 39.
 Symonds, Charles (1948): *Brit. med. J.*, **i**, 536.

rheumatic fever and is preferred by some practitioners. It is used as such or as the calcium salt, which is more soluble and less irritating to the gastric mucosa.

Dosage.—The effective dose of aspirin in rheumatic fever is roughly two-thirds that of sodium salicylate. A guide to dosage is to give 1 grain (65 mgm.) per pound body weight per day, divided into equal doses and given at three to four-hourly intervals until the fever subsides, the joint pains disappear, and the sedimentation rate returns to normal. During the past five years attention has been focused on the treatment of acute rheumatism with massive doses of aspirin or salicylates, sometimes up to 200 grains (13.3 gm.) daily. A maintained plasma salicylate level of 30 to 40 mgm. per cent. is considered essential, and frequent plasma salicylate estimations are required in the early stages, as the rates of excretion vary from time to time in any one patient.

The criterion of progress and cure is the reduction of the sedimentation rate to normal, and in several cases so treated it is claimed that the disease has been cured in so far as subsequent cardiac complications have been negligible. But the sedimentation rate is related to the plasma fibrinogen content, and in a series of cases of conditions other than rheumatic fever associated with a raised sedimentation rate treated with salicylates the sedimentation rate has been reduced to normal; it is probable that there is a specific depressant effect of salicylate on the manufacture of fibrinogen by the liver.

Observation of cases over a five-year period is probably insufficient to justify a claim of "cure" of acute rheumatism, as so often cardiac lesions are not detectable until ten years have passed since the acute infection. The exact relationship between salicylates and rheumatic fever still remains a mystery, and until this has been established the therapeutic test of aspirin or salicylates in doubtful cases of joint pains must remain as valuable as ever.

K. O. RAWLINGS, M.D., M.R.C.P.

THE ANÆSTHETIST'S BAG

THE general practitioner who gives anæsthetics will not require the same amount of apparatus as the specialist, for it is only the simpler forms of anæsthesia that the general practitioner will be expected to use. The bag should contain two sets of apparatus: first, drugs and machinery for the production of anæsthesia; and secondly, drugs and apparatus for resuscitation. No one should ever set out to give an anæsthetic, even the most simple, without the means of tackling the emergencies that might arise.

Many years ago I acceded to the request for "just a whiff of ethyl chloride, old man" in the case of an eighteen months' old child. The father and mother were old friends of mine, and both in the medical profession. A double myringotomy was to be performed, and the mother held the child. The operation was completed satisfactorily, but the child suddenly stopped breathing and collapsed. Unspoken prayers are said to be the most powerful; anyhow the child came round, but if oxygen and carbon dioxide inhalations could have been instituted at once, the recovery would have been much quicker and more certain.

It is such happenings that teach us; and as a result of this I always carry means for resuscitation even to the most trivial case. As a resident anæsthetist I once had the temerity to write some anæsthetic aphorisms: one was "Anæsthesia is full of risk"; and even to-day with all our modern methods that aphorism holds good.

APPARATUS

If possible it is well to carry a *Boyle's machine*. One of the old original Coxeter flowmeter type will be quite adequate, if provided with a Magill bag, corrugated rubber tubing, expiratory valve and facepieces, one adult's and one child's size. The gas-oxygen machine postulates a cylinder of nitrous oxide, a cylinder of oxygen, both fitted with Adams' valves, and a "J" size CO₂ sparklet. Quite extensive

Hyperpnœa.—This only occurs with a high plasma salicylate level, e.g. 30 to 40 mgm. per cent., and recent experiments have shown that this is due to direct action on the respiratory mechanism and may result in alkalosis. It can be prevented by giving sodium bicarbonate with the aspirin, which also increases the urinary excretion and lowers the plasma salicylate level.

Hypoprothrombinæmia.—This usually occurs only with more intense aspirin therapy; there is a fall in prothrombin, sufficient on occasions to lead to hæmorrhagic manifestations such as hæmatemesis, and a fatal case of hæmorrhagic encephalitis has been recorded. Vitamin K (menaphthone), 1 mgm., is sufficient to counteract 1 gm. (15 grains) of aspirin.

ASPIRIN POISONING

Approximately 50 people commit suicide annually by taking aspirin, and a much larger number makes unsuccessful attempts. The outcome largely depends upon the amount taken and the time that elapses before treatment is instituted. Death has resulted after 200 grains (13.3 gm.) in a debilitated patient, and survival is recorded after taking 1,250 grains (81 gm.); 500 grains (32.5 gm.) will be fatal in most cases if no treatment is given. The onset of symptoms after ingestion of such a dose is usually delayed for a few hours and the diagnosis depends upon (a) the mental state, which progresses from nausea and tinnitus to deafness and mental wandering, restlessness and disorientation, and finally to stupor and cerebral irritation; (b) the presence of severe perspiration; (c) the respiratory changes which may show an increase in rate with shallow or deep respiration, and (d) the finding of salicyluric acid in the urine.

Treatment, briefly, consists in:—(a) Gastric lavage with several pints of dilute sodium bicarbonate solution; (b) fluid replacement with glucose in water by mouth, or intravenous glucose-saline if the patient cannot swallow, for dehydration is a marked feature; (c) lumbar puncture; salicylate is present in the cerebrospinal fluid, and removal of up to 30 c.cm. once or twice usually produces marked improvement.

USES OF ASPIRIN

The number of conditions for which aspirin is used is enormous, and in a high proportion of these conditions it is probable that its effect is psychological rather than pharmacological. In combination with such drugs as phenacetin, caffeine and codeine it forms a good example of synergism in drug therapy; the greater part of the annual consumption of 8 cwt. of aspirin at a big London teaching hospital is used in combination with phenacetin and codeine.

In *gout*, aspirin has been shown to have a specific effect on the excretion of uric acid, sometimes augmenting the excretion by as much as 100 per cent. when used in combination with colchicum, and in consequence lowering the level of the blood uric acid.

In *infancy*, half a tablet crushed and administered in a teaspoonful of milk to a fretful child can be as soothing to the harassed parents as to the owner of the irritating gums.

Aspirin is often used in suspension in water as a *gargle* in sore throat, and in particular following tonsillectomy. There is usually rapid relief from pain, although the exact mechanism is obscure as aspirin has no local analgesic effect; it is possible that there is rapid absorption through the pharyngeal mucosa.

It is important to remember that aspirin is hydrolysed in a moist atmosphere to acetic and salicylic acids, and aspirin tablets kept in cardboard containers in bathroom cabinets soon lose their efficacy. They should always be stored in screw-capped bottles in a dry place.

ASPIRIN IN ACUTE RHEUMATISM

Aspirin appears to be as efficacious as sodium salicylate in the treatment of acute

In the second instance, the emergency may be one of *respiratory failure*, and provided the airway is clear, and the pulse good, gentle rhythmic pressure on the chest will soon start respiration again. In this emergency, the Boyle's machine is particularly useful, for the artificial respiration may be performed by manual compression of the rebreathing bag while the expiratory valve is closed. If respiratory failure is due to an overdose of thiopentone, gentle artificial respiration will prove adequate treatment if there is no gross overdose. On the other hand, it may be necessary to resort to a direct antidote. In this event, nikethamide (coramine), 5 c.cm., may be given intravenously. Respiration is usually restored almost immediately. Some anæsthetists prefer 0.3 per cent. picrotoxin, 3 c.cm. intravenously, instead of nikethamide. The picrotoxin is put up in an 0.3 per cent. solution in a rubber capped bottle.

Thirdly, there is the more dread emergency of *circulatory failure* to be considered. The acute condition with cardiac arrest calls for rapid and heroic resuscitatory measures. A Hewer's needle for intracardiac injection is a useful adjunct, and ampoules of adrenaline are necessary against this emergency. A 2 c.cm. record syringe in a spirit-proof case will prove useful for injecting the various drugs required. Chronic or gradual circulatory failure calls for replacement therapy if the condition be due to shock or hæmorrhage. It is well to have some plasma or sterile saline with sterile tubing and needle at hand. Such an outfit is marketed by Allen and Hanburys as the "sterivac".

No mention has been made of curare, spinal apparatus, or cyclopropane. These hardly come within the province of the general practitioner. On the other hand, he may be called upon to give nitrous oxide for a dentist. It is well to have a dental outfit consisting of two 50 gallon gas cylinders on a foot-piece, rubber tubing, gas bag, and suitable nosepiece for this work. The accessories required are dental props (Trewby's), Acland's gag, and possibly a boxwood wedge.

Finally, wherever the operation is to be, in private house or nursing home, always take a full 30 gallon oxygen cylinder, for it is well to remember the words of David: "Put not your trust in princes nor in any child of man".

FRANKIS EVANS, M.B., B.S., M.R.C.S., D.A., F.F.A.R.C.S.

NOTES AND QUERIES

Control of Excessive Uterine Bleeding

QUERY.—I have two young patients at the moment, suffering from excessive menstrual bleeding. This has not responded to the use of progesterone given in doses of 5 mgm. intramuscularly, twice weekly. I should be grateful if you could inform me as to which cases of excessive menstrual bleeding respond to progesterone, and in what doses the progesterone should be given.

REPLY.—Progesterone may be used in three ways to control excessive uterine bleeding:—

(1) It may be given before the expected date of bleeding. It is useless to give it before the tenth premenstrual day, in cases with a regular menstrual pattern, and a total dose of at least 40 mgm., and in some cases preferably 80 mgm., should be administered during the premenstrual week. In cases of "menorrhagia" (regular, although excessive, periods) this

treatment is often disappointing, and methyl testosterone, 15 mgm. daily for two months, more often leads to a temporary remission, sometimes lasting for six months or more.

(2) It may be given during the bleeding phase. In this case it usually increases the amount of flow during the period of administration, although the bleeding nearly always ceases within two or three days of the last injection, provided the total dose is 40 to 80 mgm. (10 or 20 mgm. should be given daily or on alternate days). A more effective method of immediately arresting the flow is to give high doses (5 mgm. four-hourly) of stilbæstrol.

(3) When bleeding occurs irregularly (at two- to twelve-week intervals) and continues in varying amounts for days, or even for weeks—a condition allied to adult "metropathia"—the excessive and irregular bleeding bouts may be prevented by giving 10 to 20 mgm. of progesterone on alternate days for 4 doses, starting

anæsthetics can be given with this type of machine, and it must be remembered that the apparatus can be used in an emergency for resuscitation. If the facepiece be firmly applied to the face and the expiratory valve closed, pressure applied to the bag by the hand can be made to inflate the lung with oxygen-carbon dioxide mixture in the event of respiratory failure.

A *Bellamy Gardner wire mask*, adult's and child's, covered with gauze or house flannel, is advisable for open ether or ethyl chloride. A Bellamy Gardner dropper for ether is recommended for use in conjunction with this. A Mills's chloroform drop bottle, two ounce size, together with lint which can be cut to make a Bart's lint, is useful if chloroform is to be used. A bottle of ether, chloroform, trichloroethylene and a tube of ethyl chloride, are really all that is required as volatile narcotics, unless perhaps some di-vinyl ether (vinesthene) be added as a refinement.

Accessories are advisable as follows:—

Two airways, one adult's and one child's. The Phillips's pattern is preferable as an all-round airway, for the Guedel pattern is not suitable for every patient.

A *Mason's*, *Fergusson's*, or *Acland's gag* is always useful, but tongue forceps should never be used. If it be necessary to pull the tongue forward, a *Lack's tongue depressor* will be found suitable. In this event the instrument is used the wrong way round in that the handle is placed on the tongue so that the little curve at the end serves to pull the tongue forward.

Now comes the question of *endotracheal apparatus* and the Magill or Macintosh laryngoscope. Strictly speaking, the general practitioner cannot be expected to pass endotracheal tubes, but some there are who have had experience in the art, and therefore they will certainly carry this apparatus with them. I do not intubate children as a rule, and I recommend that Magill's tubes in sizes 2 to 7 inclusive will prove adequate. A Magill's laryngoscope with detachable blades should be sufficient, and a spare bulb and battery are recommended.

INTRAVENOUS ANÆSTHESIA

A 20 c.cm. record syringe with eccentric nozzle in a spirit-proof case is recommended, together with filling needle and intravenous needles. These should be short and should have a short bevel with a sharp point. I favour thiopentone as pentothal, and both half and one gramme sizes should be carried. A piece of soft rubber tubing should be carried to act as a tourniquet, and a separate bottle containing spirit is an advantage for preparing the skin.

RESUSCITATION AND EMERGENCIES

Measures for resuscitation fall into three categories:—

First must be considered the question of *respiratory obstruction*, which will become respiratory failure if it is not relieved quickly. Often the cause of obstruction is the tongue held closely against the teeth of a tightly clenched jaw. This presents a difficult problem, for the attempt to open the jaw by means of a gag is fraught with risk to the teeth, and it is likely that if the mouth be opened the patient will not stand an airway without a cough or even spasm of the larynx. This is the situation when a *short* Magill catheter (no. 5 or even no. 4) passed down the nose just to the back of the tongue will give prompt and adequate relief. In the case of respiratory obstruction due to the tongue falling back and blocking the airway, the insertion of an airway will be all that is required. Respiratory obstruction due to complete spasm of the laryngeal cords may even necessitate laryngotomy or tracheotomy. When there is acute oedema of the larynx it may be extremely difficult to pass an endotracheal tube as an emergency measure, so that it is well to carry a laryngotomy set against sudden necessity. The practitioner may never need to use it, but if it is not at hand, he may one day be faced with a death which need not have happened.

constant correction or ridicule are usually the cause of this second stage, for which the parents are often responsible, either by applying the "remedy" themselves or by allowing others to do so. The mother can help by keeping the child as quiet as possible. A mid-day rest and an early bedtime are essential. Nursery rhymes treated as a game can be most helpful at this stage, especially if they are done with a certain amount of action. This not only amuses the child but helps to instil into her a sense of rhythm and enjoyment of actual speech. These action rhymes distract the child's mind from the fear of words. It does not necessarily follow that a stammering father has a stammering child, but if the parents are over-anxious about the tendency to inherit, they may fix the "physiological stammer" into a true one. I would suggest that the father should consult a speech therapist with regard to his own condition, as this will not only alleviate his trouble, but will show him how to handle his own child.

E. J. BOOME, M.D., M.R.C.P., D.P.H.

Inoculation of Infants

QUERY.—Will you please inform me whether it is necessary for a baby of about eight to ten months old to have any T.A.B. or cholera vaccine before going to the Sudan? The child has of course been vaccinated against smallpox.

REPLY.—Nowadays intending travellers before deciding about protective inoculations for themselves and their families should first ascertain the requirements of the shipping company or air line by which the journey is to be made, and also the official requirements of the country of destination. This having been done special personal risks and susceptibilities can be considered.

In this particular instance it is unlikely that the shipping company or air line will require anything more than vaccination against smallpox, which for the time being is the only official requirement of the Sudan government.

The risk of food- and water-borne disease run by an infant of nine months in the Sudan will depend upon local circumstances, but if the amenities are those customary in a European establishment in that country it should not be much greater than in Great Britain. Generally speaking it is not regarded as necessary to inoculate infants under eighteen months against enteric fever unless there are special circumstances, e.g., a known typhoid carrier in the household. When it is desired to protect against such special risks, a T.A.B.C. vaccine (alcohol killed), diluted to a strength suitable for the inoculation of infants, which is sold by Allen and Hanbury's, can be recommended as unlikely

to cause reactions. The routine inoculation of infants going to the Sudan against cholera is not at present thought to be necessary.

E. T. CONYBEARE, M.D., F.R.C.P.

The Wintrobe Hæmatocrit Technique

QUERY.—In the September issue of *The Practitioner* mention is made by D. H. Collins of the use of the Wintrobe tube for hæmatocrit reading. He advises the use of ammonium oxalate 6 mgm., and potassium oxalate 4 mgm., to 5 c.cm. blood. I would be glad to know if this oxalate mixture can be obtained in any convenient form, e.g. tablets? Also where electricity is not available would a car propeller with tube strapped on serve as a centrifuge?

REPLY.—Tubes for anticoagulant are conveniently prepared as follows:—

Obtain a stock solution containing 6 gm. of ammonium oxalate and 4 gm. of potassium oxalate per 100 c.cm. of distilled water. Add 0.1 c.cm. (i.e. 2 drops from a dripping bottle) to each clean dry tube. Evaporate to dryness either over a small flame or in the kitchen oven with the tubes lying flat. The latter is convenient if many tubes are being prepared at the same time.

The only satisfactory alternative to an electric centrifuge is a water driven one. This is a highly efficient instrument if the buckets are large enough to hold the Wintrobe tube. Strapping the tube to a car propeller will not do; I have tried it and the tube smashes before proper speeds are obtained.

D. H. COLLINS, O.B.E., M.D.

Dirty Bank Notes and Infection

QUERY.—Could you inform me whether there is any risk of acquiring infection from the large number of dirty bank notes which are now circulating? If so, are there any simple precautions which should be taken to avoid this? I am prompted to ask this question as I have recently been told by a bank clerk that an infection of his skin was attributed to such infection.

REPLY.—There is virtually no risk of acquiring an infection of the skin through handling dirty bank notes. E. W. PROSSER THOMAS, M.D.

Treatment of Halitosis

DR. P. T. K. NAYAR (*Alor Star, Malaya*) writes:—"Regarding halitosis, about which an article appeared in the August issue (p.140), may I suggest that the majority of cases originate in a deficient secretion of saliva? In these cases the saliva is thick and stagnates in the mouth, and the halitosis is apparent two or three hours after a meal. The rational treatment is to stimulate the salivary secretion by chewing gum or by sucking sweets when the halitosis appears".

arbitrarily during the non-bleeding phase, and repeating the course every 28 days. The total dose of 40 to 80 mgm. leads to a progesterone withdrawal bleeding which resembles a normal period in amount and duration. Such bleedings result in complete shedding of the endometrium, and have been referred to as a "medical D. and C.". This complete endometrial shedding prevents the building up of a hyperplastic endometrium from which the excessive and protracted bleeding of the metropathic phase takes place. This method is usually dramatically successful.

In all these cases it is important to achieve a total dose of at least 40 mgm. within a week, and it is therefore understandable that doses of 5 mgm. twice weekly were ineffective in the two cases cited.

P. M. F. BISHOP, D.M.

Treatment of Vitiligo

QUERY (from S. Africa).—I would be grateful for any information on current views concerning the treatment of vitiligo. About a year ago I saw an Indian child, aged eight years, with extensive patches on the back, buttocks and thighs, of approximately five years' duration. Purely empirically, I gave this patient weekly intramuscular injections of 2 c.cm. of adrocortin (an adrenal cortical extract prepared in South Africa), for a period of six months. Attendance was not absolutely regular, but the results have been surprisingly satisfactory. Almost 100 per cent. repigmentation of the patches occurred. I am now treating an elder sister, aged fourteen, with a similar condition of the vulva, the dose being increased to 4 c.cm., and there appears to be beginning improvement. I would much appreciate an opinion on the above subject.

REPLY.—The treatment of vitiligo is unsatisfactory at present and is likely to be so while the etiology remains obscure. Suprarenal cortical extract has been used before, with disappointing results. Vitiligo is occasionally an early sign of Addison's disease and may also disappear spontaneously. The efficacy of this form of treatment is therefore difficult to assess. Vitiligo with onset at the menopause may respond to oestrogen therapy in the female and similarly to testosterone in the male. In the younger age-groups cosmetic treatment with stains prepared from green walnut husks, tincture of iodine, and 0.2 to 0.5 per cent. aqueous potassium permanganate solution is useful. The white patches are coloured to match the pigmented border. The pigmented areas can be rendered less obvious with calamine lotion, tinted with sulphonated bitumen or with

"covermark", or partially bleached by strong hydrogen peroxide in lanolin or 1 per cent. mercuric chloride in a 20 per cent. spirit lotion.

Improvement has resulted from exposure of the white patches to the Kromayer lamp. Ultra-violet light exposure combined with local painting of the depigmented areas with 10 per cent. alcoholic solution of oil of bergamot or with gold injections, may produce partial repigmentation. Para-amino-benzoic acid, 100 mgm. t.d.s., with large doses of vitamin B complex and ascorbic acid have recently been tried. Depigmented patches in exposed areas should be protected from bright sunlight by a sun screen, such as 10 per cent. salol in yellow soft paraffin, or severe sunburn may result.

P. D. C. KINMONT, M.B.E., M.D., M.R.C.P.

Treatment of Vaginitis

QUERY.—I shall be grateful for advice on the treatment of a patient with vaginitis. The laboratory report shows that *Monilia albicans* and scanty pus cells are present in the smears. Neither *Trichomonas* nor gonococci were found. Treatment has included S.V.C. tablets, gentian violet pessaries, oil douches, and penicillin—all without effect. Can you suggest a line of treatment?

REPLY.—First I would suggest painting the vaginal walls, after drying, with a 1 per cent. aqueous solution of gentian violet, on alternate days for six applications. On the other days insert an iodox vaginal pessary the last thing at night. If this treatment fails, try painting with tincture of iodine for a similar number of times at similar intervals, using the iodox pessary in between.

ARTHUR GRAY, M.D., F.R.C.S., F.R.C.P., F.R.C.O.G.

Stammering in Childhood

QUERY.—I shall be grateful for advice concerning the prognosis and treatment in the case of a healthy child, aged three years, who developed a stammer twelve months ago. She is an only child and is both precocious and impulsive. Her father stutters badly.

REPLY.—At the initial stage of speech development the mental process is in advance of the powers of muscular control, and the resulting lack of muscular coordination often produces a temporary stammer. Many children begin speech with a so-called "physiological" stammer. If the child is worried or nervous during this period of adjustment she will become conscious of her speech and the difficulties surrounding its acquisition, and at once the second stage is reached—that of fear or dread of speech—unconscious probably but none the less potent. Too much attention to the initial difficulties and

constant correction or ridicule are usually the cause of this second stage, for which the parents are often responsible, either by applying the remedy themselves or by allowing others to do so. The mother can help by keeping the child as quiet as possible. A mid-day rest and an early bedtime are essential. Nursery rhymes treated as a game can be most helpful at this age, especially if they are done with a certain amount of action. This not only amuses the child but helps to instil into her a sense of rhythm and enjoyment of actual speech. These action rhymes distract the child's mind from the fear of words. It does not necessarily follow that a stammering father has a stammering child, but if the parents are over-anxious about the tendency to inherit, they may fix the "physiological stammer" into a true one. I would suggest that the father should consult a speech therapist with regard to his own condition, as his will not only alleviate his trouble, but will show him how to handle his own child.

E. J. BOONE, M.D., M.R.C.P., D.P.H.

Inoculation of Infants

QUERY.—Will you please inform me whether it is necessary for a baby of about eight to ten months old to have any T.A.B. or cholera vaccine before going to the Sudan? The child has of course been vaccinated against smallpox.

REPLY.—Nowadays intending travellers before deciding about protective inoculations for themselves and their families should first ascertain the requirements of the shipping company or air line by which the journey is to be made, and also the official requirements of the country of destination. This having been done special personal risks and susceptibilities can be considered.

In this particular instance it is unlikely that the shipping company or air line will require anything more than vaccination against smallpox, which for the time being is the only official requirement of the Sudan government.

The risk of food- and water-borne disease run by an infant of nine months in the Sudan will depend upon local circumstances, but if the amenities are those customary in a European establishment in that country it should not be much greater than in Great Britain. Generally speaking it is not regarded as necessary to inoculate infants under eighteen months against enteric fever unless there are special circumstances, e.g., a known typhoid carrier in the household. When it is desired to protect against such special risks, a T.A.B.C. vaccine (alcohol killed), diluted to a strength suitable for the inoculation of infants, which is sold by Allen and Hanburys, can be recommended as unlikely

to cause reactions. The routine inoculation of infants going to the Sudan against cholera is not at present thought to be necessary.

E. T. CONYBEARE, M.D., F.R.C.P.

The Wintrobe Hæmatocrit Technique

QUERY.—In the September issue of *The Practitioner* mention is made by D. H. Collins of the use of the Wintrobe tube for hæmatocrit reading. He advises the use of ammonium oxalate 6 mgm., and potassium oxalate 4 mgm., to 5 c.cm. blood. I would be glad to know if this oxalate mixture can be obtained in any convenient form, e.g. tablets? Also where electricity is not available would a car propeller with tube strapped on serve as a centrifuge?

REPLY.—Tubes for anticoagulant are conveniently prepared as follows:—

Obtain a stock solution containing 6 gm. of ammonium oxalate and 4 gm. of potassium oxalate per 100 c.cm. of distilled water. Add 0.1 c.cm. (i.e. 2 drops from a dripping bottle) to each clean dry tube. Evaporate to dryness either over a small flame or in the kitchen oven with the tubes lying flat. The latter is convenient if many tubes are being prepared at the same time.

The only satisfactory alternative to an electric centrifuge is a water driven one. This is a highly efficient instrument if the buckets are large enough to hold the Wintrobe tube. Strapping the tube to a car propeller will not do; I have tried it and the tube smashes before proper speeds are obtained.

D. H. COLLINS, O.B.E., M.D.

Dirty Bank Notes and Infection

QUERY.—Could you inform me whether there is any risk of acquiring infection from the large number of dirty bank notes which are now circulating? If so, are there any simple precautions which should be taken to avoid this? I am prompted to ask this question as I have recently been told by a bank clerk that an infection of his skin was attributed to such infection.

REPLY.—There is virtually no risk of acquiring an infection of the skin through handling dirty bank notes. E. W. PROSSER THOMAS, M.D.

Treatment of Halitosis

DR. P. T. K. NAYAR (*Alor Star, Malaya*) writes:—"Regarding halitosis, about which an article appeared in the August issue (p.140), may I suggest that the majority of cases originate in a deficient secretion of saliva? In these cases the saliva is thick and stagnates in the mouth, and the halitosis is apparent two or three hours after a meal. The rational treatment is to stimulate the salivary secretion by chewing gum or by sucking sweets when the halitosis appears".

PRACTICAL NOTES

Penicillin in the Treatment of Abscesses

As a result of his experience of 15 children with abscesses in various parts of the body, H. J. Cohen (*Journal of American Medical Association*, August 21, 1948, 137, 1531) recommends the following treatment. Penicillin is given, preferably in solution by the intramuscular route every three hours, for a few days until the infection becomes localized. When fluctuation is evident, aspiration is performed, using a "20 c.cm. Luer syringe attached to a $1\frac{1}{2}$ inch (3.8 cm.) 18 gauge needle". After aspiration is complete, the needle is left *in situ* and a fresh syringe attached to it containing a solution of penicillin (25,000 units per c.cm.) in isotonic sodium chloride. The penicillin is injected until the cavity is distended. The needle is then removed and firm pressure is applied for about a minute to prevent escape of any of the penicillin. On the average, 3 to 5 c.cm. of pus was usually removed and replaced by the same volume of penicillin solution. As a rule only one such treatment was necessary, and after about a week the mass subsided. The advantages of the method are said to be that it can be easily performed without anaesthesia in the patient's home, that it reduces the amount of nursing care necessary, avoids the need for repeated painful changes of dressings, and prevents scar formation. All the 15 children were cured, and in none was any subsequent incision or drainage required.

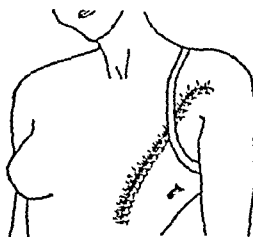
Ruptured Quadriceps

RUPTURE of the quadriceps femoris almost always occurs in heavy elderly men as a result of indirect violence, e.g., a missed foothold while going downstairs. In a review of the subject Eric I. Lloyd (*British Journal of Surgery*, July 1948, 36, 94) points out that the characteristic clinical features are inability to extend the knee and a palpable depression in the surface of the extensor tendon. Treatment is surgical and should be carried out as soon as possible after the accident, although a delay of a day or so does not usually interfere with the result. The operation for repair of the rupture should be carried out under a general anaesthetic, and it is important that a tourniquet should not be used during the operation as this increases the risk of postoperative pulmonary embolism. Suture is worth while up to three months after the rupture. The important feature of post-operative care is that the patient should be

encouraged to move about in bed as much as possible and to exercise the toes and ankle in the affected limb regularly. This is to reduce the risk of pulmonary embolism, which is particularly liable to occur in these patients as they are often over the age of seventy. Four or five days after operation static exercises with the quadriceps are begun. The stitches are removed on the tenth day, and the patient is allowed up on the following day, walking about with the aid of a stick. The plaster is removed six weeks after operation. The results of operation are described as "excellent" if operation is performed soon after rupture, and "fairly satisfactory" in those operated upon within three months of the injury.

A Postoperative Mastectomy Dressing

A SIMPLE and effective postoperative dressing for a radical mastectomy wound is described by L. H. Pollock (*New England Journal of Medicine*, September 2, 1948, 239, 366). A strip of plain or elastic adhesive plaster is flamed, and starting over the lower aspect of the scapula the strap is brought across the axilla by one hand while the other hand presses the posterior axillary fold anteriorly and upward. The medial or upper skin flap is pushed towards the incision as the strap is carried upwards in the infraclavicular depression resulting from removal of the pectoral muscles. The strap is then brought across the ridge of the shoulder and ends over the upper part of the scapula. A thin piece of gauze can be placed over the incision under the adhesive plaster.



Curved adhesive strap, moulding the skin to the chest wall in a longitudinal incision. This supports the posterior axillary fold to lessen the tension on the suture line. It greatly decreases the padding needed to obliterate the dead space.

The advantage of this method is stated to be "the selective moulding of the skin to the concavity in front of the head of the humerus before the outer dressings are applied." This is shown in the accompanying figure. Minimization of padding to obliterate the post-operative space; support of the weight of the pos-

terior axillary fold (which may be considerable in an obese or muscular patient), and lessening of the circular constrictions on the chest, as when

bandages of broad adhesive transverse straps are employed, are other points stated to be in favour of the method. A similar curved adhesive strip can be placed over any padding. It is also claimed that the method assists healing by helping to approximate the edges and decreasing the oedema of skin and tissue. It is not necessary to remove the outer dressings to take out the drain: "a heavy silk suture may be attached to the end of the drain and then fastened lineally to the lower edge of the outer pad. The drain may be extracted by pulling on the loose end of the thread".

Anticoagulant Therapy and the Erythrocyte Sedimentation Rate

IN view of the difference of opinion as to the effect of heparin and dicoumarol upon the erythrocyte sedimentation rate, Stuart W. Cosgriff (*Journal of Clinical Investigation*, July 1948, 27, 435) has re-investigated the problem in a series of patients, in all of whom the sedimentation rate had been static for a period of time before the start of the investigation. The effect of heparin was investigated in 10 patients, dicoumarol in 10, and heparin plus dicoumarol in 5 patients. In the dosage usually administered clinically, neither heparin nor dicoumarol, nor the two combined, had any significant effect upon the sedimentation rate. It is therefore concluded that "the erythrocyte sedimentation rate of a patient receiving anticoagulant therapy can be considered to be as reliable a guide in the management of such an individual as it is in patients not receiving anticoagulants".

The Topical Application of Benadryl

BECAUSE of the frequency of side-effects resulting from the oral administration of benadryl, T. H. McGavack *et al.* (*Archives of Dermatology and Syphilology*, March 1948, 57, 308) investigated its action when used as an ointment. Two different formulae were used—

Ointment 1	Benadryl	5 per cent
	Water	10 per cent
	Wool fat, anhydrous, odourless	15 per cent
	White petrolatum	70 per cent

Ointment 2	Benadryl	2 per cent
	"Carbowax 1,500" mono-stearate	to 100 per cent

Ointment 1 was used in 56 patients with itching dermatoses. Itching was completely relieved in 32 cases, partially relieved in 16, and uninfluenced in the remainder. The duration of relief from a single application of the ointment varied considerably. Improvement was usually noticed in 5 to 15 minutes and lasted from a half to several hours. Of eight patients

in whom the ointment base was applied to one set of lesions and the complete ointment to another set of lesions, seven considered that improvement was more marked with the ointment containing the benadryl. Untoward reactions were encountered in six patients, and in one of these it was due to the wool fat. Ointment 2 was applied to 18 patients with itching dermatoses, and 14 of them obtained complete or partial relief. Irritation of the skin was noted in only one patient to whom ointment 2 was applied. As ointment 2 appeared to be as effective as ointment 1 and to be less irritating, it is concluded that it is probably the preferable one to use. In none of the patients were any systemic side-effects observed from the application of the ointments to broken or intact skin.

Sodium Acid Phosphate in the Control of Urinary Calculi

THREE main factors are said to be concerned in the production of urinary calculi which is so liable to occur in patients kept in the recumbent position for prolonged periods: (1) stasis; (2) infection; (3) hypercalcaemia. J. J. Cordonnier and B. S. Talbot (*Journal of Urology*, August 1948, 60, 316), who found the average daily excretion of calcium to be 310 mgm. in 71 recumbent patients, and 223 mgm. in 20 ambulatory controls, have investigated the effect of the ingestion of sodium acid phosphate on this hypercalcaemia in 16 recumbent patients. The patients, all of whom had normal serum calcium and phosphorus levels, were given 5.8 gm. of sodium acid phosphate daily for ten days. In every case there was a definite reduction in urinary calcium. The average output before the administration of sodium acid phosphate was 366 gm., compared with 189 gm. after the course was completed. Details are given of one patient, aged twenty-two years, with urinary symptoms of four months' duration, and in whom a diagnosis of incrustated cystitis was made. There was hypercalcaemia. After the administration of sodium acid phosphate the urinary calcium returned to normal and the incrustations disappeared.

Tetraethylammonium Chloride in Hypertension

A COMPARISON of the relative value of sodium amytal and tetraethylammonium chloride in the selection of hypertensive patients for sympathectomy has been made by I. G. Tamagna and C. A. Poindexter (*American Journal of Medical Sciences*, June 1948, 215, 651).

Sodium amytal was given orally in doses of 3 grains (0.2 gm.) hourly for three doses, and the blood pressure

was taken at 30 minute intervals for four to six hours. Tetraethylammonium chloride was given slowly by the intravenous route—2 c.cm. (0.2 mgm.) over a period of 1 to 1½ minutes. The blood pressure was recorded at 30 second intervals during the injection, and then at 1 minute intervals until the control level was reached. The lowest level was reached about 10 minutes after the injection.

The two tests were compared in 68 hypertensive patients. In 51 patients the fall in blood pressure produced by the two tests varied by less than 15 mm. Hg, in 13 cases by 15 to 30 mm., and in four by more than 30 mm. Hg. Of these last four patients, three had malignant hypertension, and in them the fall in diastolic pressure produced by tetraethylammonium chloride ranged from 75 to 90 mm. Hg, compared with 30 to 40 mm. Hg with sodium amylal. In the fourth patient there was a greater fall in the diastolic pressure with sodium amylal than with tetraethylammonium chloride, and this may have been explained by the fact that in this patient the injection of tetraethylammonium chloride was painful because of poor technique. The side-effects of tetraethylammonium chloride were negligible, and in no case was the electrocardiogram affected by either agent. It is concluded that tetraethylammonium chloride is a safe and more specific agent for the preoperative evaluation of hypertensive patients for sympathectomy. Sodium amylal depresses the blood pressure by depression of the central nervous system, whereas tetraethylammonium chloride produces a specific paralysing action in the structures removed by thoraco-lumbar sympathectomy. A further advantage of tetraethylammonium chloride is that results are obtained within 30 minutes, compared with five hours in the case of sodium amylal.

Music as an Adjunct to Dental Anæsthesia

"In order to reduce the amount of nitrous oxide and its attendant oxygen deprivation as prevalently practiced in dentistry", H. Cherry and I. M. Pallin (*Anæsthesiology*, July 1948, 9, 391) recommend the use of music. The most effective music for this purpose "had a smooth even tone and contained no complicating harsh or startling instrumentation". In a series of over 1000 cases the most effective records were found to be those of Debussy's "Chair de Lune", Beethoven's "Moonlight Sonata", Humperdinck's "Dream Pantomime", Wagner's "Evening Star" and "Forest Murmurs", and Fibich's "Poème". The equipment which was used, consisted of an ordinary electric record player with earphone transmission instead of the usual loudspeaker. The earphones had large cups to exclude environmental sounds, and a microphone was interconnected so that the operator

could talk at any time to the patient. There was also a remote volume control so that the patient could adjust the volume to his own liking. The actual anæsthetic procedure consisted in the patient being comfortably settled in the dental chair with the music adjusted as required. A nasal inhaler mask was then adjusted and the anæsthetic machine set to deliver 75 per cent. nitrous oxide and 25 per cent oxygen. The additional advantages claimed for this method are that it facilitates smooth induction of anæsthesia, abolishes retching and vomiting, and facilitates recovery from the anæsthetic.

The Radiological Diagnosis of Gall-Bladder Disease

THE results in 500 consecutive patients referred for cholecystographic study have been analysed by F. Greenwood and E. Samuel (*British Journal of Radiology*, September 1948, 21, 438). A standard proprietary radio-opaque substance given orally was used in all cases. Of 382 cases finally proved to be normal, 36 (9.9 per cent.) were regarded as pathological with a single dose, but were shown to function normally with two further doses. It is therefore recommended that in all cases in which a single dose does not show a normally filled gall-bladder the three-dose technique should be adopted. Of 94 cases revealing positive evidence of gall-stones, 33 (35.1 per cent.) showed gall-stones on the control film. Of the remaining 61, 11 (18 per cent.) were demonstrable only in the erect position. It is therefore urged that "screening of the gall-bladder in the erect position using serial radiography and compression is essential in every examination of the gall-bladder". This technique, among other things, minimizes the bowel shadows which can be so confusing in such cases. In cases in which bowel shadows are particularly confusing, tomography may conclusively demonstrate gall-stones.

A Cream for Brittle Nails

IN an article dealing with a dermatological formulary, H. Goodman (*Merck Report*, July 1948, 57, 14) gives the following formula of a cream for brittle nails:—

Lanolin, anhydrous	30
Peach-kernel oil	6
Corn oil	2
Castor oil	2
Beeswax, yellow	4
Cetyl alcohol	2
Borax	1
Water, sufficient to make	100

Melt the fat-like solids, warm the oils, heat the water with borax, and stir, utilizing mechanical agitation until cream forms.

REVIEWS OF BOOKS

Emergencies in Medical Practice. EDITED BY C. ALLAN BIRCH, M.D., F.R.C.P. Edinburgh: E. & S. Livingstone Ltd., 1948. Pp. vi and 468. Figures 113. Price 25s.

His book by a number of contributors deals in a practical manner with the emergencies of practice. Each chapter is devoted to some particular type of disorder and the practitioner will find real practical help when he looks for advice. Not only are the emergencies of ordinary practice at home considered, but there are sections dealing with medical emergencies at sea and in the air, whilst medico-legal problems also receive attention. This book is recommended to all practitioners, and it will be of especial value to those who practice in remote places, in the Services and at sea, where there is no colleague to call and few books in which to seek advice. The book is handsomely produced and both well and usefully illustrated.

British Surgical Practice. Volumes 2 and 3. EDITED BY SIR ERNEST ROCK CARLING, F.R.C.P., F.R.C.S., and J. PATERSON ROSS, M.S., F.R.C.S. London: Butterworth & Co. (Publishers) Ltd, 1948. Pp. xxviii and 540; xxxvi and 524. Figures 318 and 287. Plates 4. Price 60s. per volume.

THE second and third volumes of *British Surgical Practice* reach the same high standard as the first—high praise indeed—and they allow the reader to judge even better the scheme of the work as a whole. The general style of printing and the choice and reproduction of the illustrations are as good as they could be, the abundant series of skiagrams illustrating the six articles on the surgery of the brain will be a revelation to most readers of the details that can now be demonstrated by the expert in this branch of radio-diagnosis. As in volume I, many of the articles are by specialists other than surgeons. The allocation of general subjects, such as backache, blood pressure, errors of bone development and growth, and metabolic dystrophies in bone, to such acknowledged authorities as Henry Cohen, Geoffrey Evans, R. W. B. Ellis and Donald Hunter, shows real wisdom on the part of the Editor. Ellis gives an account of developmental rarities, beautifully illustrated, that will be the classic article on this subject. Hunter, as the leading authority on calcium metabolism, writes with authority but his use of the term "focal osteitis fibrosa" for

a group that seems to include giant cell tumours and solitary bone cysts is confusing. The whole series of articles on bones, which includes discussions on grafting by B. H. Burns and on tumours by Sir Harry Platt, is excellent. Equally good is the series on the brain, among which the chapter on head injuries by E. H. Botterill, on investigation by D. W. C. Northfield, and on their operative treatment by Sir Hugh Cairns deserve special mention. Volume III goes as far as E, a letter that seems to be appropriated by specialists. It has the chapters on endoscopy, the ear, and the eye, and therefore contains a number of articles that will be of the greatest value to the general surgeon working in isolation. Any surgeon who seeks complete and authoritative information on any subject that concerns his work, and which starts with B, C, D, or E, will find it in these volumes.

Treatment of Heart Disease. BY WILLIAM A. BRAMS, M.S., M.D., PH.D. Philadelphia and London: W. B. Saunders Co., 1948. Pp. vi and 195. Figures 11. Price 17s. 6d.

THIS is a useful, sound and practical exposition of the subject. It has the further advantage of being based upon the author's personal experience, so that it avoids the all too common practice of modern textbooks of being nothing more than a mere catalogue of current practice. The author has wisely described the methods which in his own practice he has found to be of value. The teaching throughout is sound and practical, but it is surprising to find the oxygen tent given priority over the B.L.B. mask. On the other hand, it is refreshing to find strophanthine coming back into its own. A particularly useful feature of this book is that the initial chapter is devoted to a review of the pharmacological action of drugs used in the treatment of heart disease. There is a useful bibliography of 290 references which is reasonably representative of American and British publications. This is a textbook which general practitioners and medical students will find of real value.

Pathological Processes in Malaria and Blackwater Fever. BY BRIAN MAEGRAITH, M.B., D.Phil., B.Sc., Oxford: Blackwell Scientific Publications, 1948. Pp. xi and 430. Figures 22. Price 35s.

TWENTY years ago the pathology of malaria was described in practically a single sentence—blockage of capillaries by parasitized erythrocytes. Recent studies in which the author has played a notable part have shown that the

was taken at 30 minute intervals for four to six hours. Tetraethylammonium chloride was given slowly by the intravenous route—2 c.cm. (0.2 mgm.) over a period of 1 to 1½ minutes. The blood pressure was recorded at 30 second intervals during the injection, and then at 1 minute intervals until the control level was reached. The lowest level was reached about 10 minutes after the injection.

The two tests were compared in 68 hypertensive patients. In 51 patients the fall in blood pressure produced by the two tests varied by less than 15 mm. Hg, in 13 cases by 15 to 30 mm., and in four by more than 30 mm. Hg. Of these last four patients, three had malignant hypertension, and in them the fall in diastolic pressure produced by tetraethylammonium chloride ranged from 75 to 90 mm. Hg, compared with 30 to 40 mm. Hg with sodium amylal. In the fourth patient there was a greater fall in the diastolic pressure with sodium amylal than with tetraethylammonium chloride, and this may have been explained by the fact that in this patient the injection of tetraethylammonium chloride was painful because of poor technique. The side-effects of tetraethylammonium chloride were negligible, and in no case was the electrocardiogram affected by either agent. It is concluded that tetraethylammonium chloride is a safe and more specific agent for the preoperative evaluation of hypertensive patients for sympathectomy. Sodium amylal depresses the blood pressure by depression of the central nervous system, whereas tetraethylammonium chloride produces a specific paralyzing action in the structures removed by thoraco-lumbar sympathectomy. A further advantage of tetraethylammonium chloride is that results are obtained within 30 minutes, compared with five hours in the case of sodium amylal.

Music as an Adjunct to Dental Anæsthesia

"IN order to reduce the amount of nitrous oxide and its attendant oxygen deprivation as prevalently practiced in dentistry", H. Cherry and I. M. Pallin (*Anesthesiology*, July 1948, 9, 391) recommend the use of music. The most effective music for this purpose "had a smooth even tone and contained no complicating harsh or startling instrumentation". In a series of over 1000 cases the most effective records were found to be those of Debussy's "Clair de Lune", Beethoven's "Moonlight Sonata", Humperdinck's "Dream Pantomine", Wagner's "Evening Star" and "Forest Murmurs", and Fibich's "Poème". The equipment which was used, consisted of an ordinary electric record player with earphone transmission instead of the usual loudspeaker. The earphones had large cups to exclude environmental sounds, and a microphone was interconnected so that the operator

could talk at any time to the patient. There was also a remote volume control so that the patient could adjust the volume to his own liking. The actual anæsthetic procedure consisted in the patient being comfortably settled in the dental chair with the music adjusted as required. A nasal inhaler mask was then adjusted and the anæsthetic machine set to deliver 75 per cent. nitrous oxide and 25 per cent. oxygen. The additional advantages claimed for this method are that it facilitates smooth induction of anæsthesia, abolishes retching and vomiting, and facilitates recovery from the anæsthetic.

The Radiological Diagnosis of Gall Bladder Disease

THE results in 500 consecutive patients referred for cholecystographic study have been analysed by F. Greenwood and E. Samuel (*British Journal of Radiology*, September 1948, 21, 438). A standard proprietary radio-opaque substance given orally was used in all cases. Of 382 cases finally proved to be normal, 36 (9.9 per cent.) were regarded as pathological with a single dose but were shown to function normally with two further doses. It is therefore recommended that in all cases in which a single dose does not show a normally filled gall-bladder the three dose technique should be adopted. Of 94 cases revealing positive evidence of gall-stones, 31 (35.1 per cent.) showed gall-stones on the control film. Of the remaining 63, 11 (18 per cent.) were demonstrable only in the erect position. It is therefore urged that "screening of the gall-bladder in the erect position using serial radiography and compression is essential in every examination of the gall-bladder". This technique, among other things, minimizes the bowel shadows which can be so confusing in such cases. In cases in which bowel shadows are particularly confusing, tomography may conclusively demonstrate gall-stones.

A Cream for Brittle Nails

IN an article dealing with a dermatological formula, H. Goodman (*Merck Report*, July 1948, 57, 14) gives the following formula of a cream for brittle nails:—

Lanolin, anhydrous	30
Peach-kernel oil	6
Corn oil	2
Castor oil	2
Beeswax, yellow	4
Cetyl alcohol	2
Borax	1
Water, sufficient to make	100

Melt the fat-like solids, warm the oils, heat the water with borax, and stir, utilizing mechanical agitation until cream forms.

NEW EDITIONS

Clinical Laboratory Methods, Vols. 1, 2 and 3, by R. B. H. Gradwohl, M.D., D.Sc., F.R.S.T.M. & H., in its fourth edition (C. V. Mosby Company, St. Louis, \$40, the 3 volumes) has been greatly extended in all sections for the inclusion of new material. A new chapter on electrocardiography has been included. The third volume is devoted entirely to parasitology and tropical medicine. The new edition is beautifully produced and illustrated.

Recent Advances in Obstetrics and Gynaecology, by Aleck W. Bourne, M.B., B.Ch., F.R.C.S., F.R.C.O.G., and Leslie H. Williams, M.D., M.S., F.R.C.S., F.R.C.O.G., in its seventh edition (J. & A. Churchill Ltd., 21s.) contains six new chapters, including one on the anæmias of pregnancy, by Professor L. J. Davis, and another on penicillin in obstetrics.

Pharmacology, by J. H. Gaddum, Sc.D., F.R.S., M.R.C.S., L.R.C.P., in its third edition (Oxford University Press, 25s.) contains among the new additions, sections on folic acid, streptomycin, penicillin, the antihistamine drugs, BAL and the new insecticides. In the chapter on the blood, sections are devoted to the anticoagulants, heparin and dicoumarol.

The fourth edition of *The Radiology of Bones and Joints*, by James F. Brailsford, M.D., Ph.D., F.R.C.P., F.I.C.S. (J. & A. Churchill Ltd., 63s.) contains 615 illustrations, most of which are reproductions of skiagrams. They are beautifully produced, and with the guidance of the explanatory text should prove of great value, not only to radiologists but also to practitioners, in the diagnosis of diseases and abnormalities of the bones.

The sixth edition of *Treatment in General Practice*, by Harry Beckman M.D. (W. B. Saunders Co., Ltd., 57s. 6d.) contains sections on a number of new subjects, including Loeffler's syndrome, coccidiosis, moniliasis, rickettsial pox, Reiter's syndrome, mite infestation, and the management of penicillin reactions. Of chemotherapeutic agents, streptomycin, penicillin, the sulphonamides, the antihistamine drugs, and BAL are among those of which detailed description is given. This is a comprehensive practical textbook.

Malignant Disease and its Treatment by Radium, Vol. 1, by Sir Stanford Cade, K.B.E., C.B., F.R.C.S., M.R.C.P., in its second edition (John Wright & Sons, Ltd., 52s. 6d.) is to be divided into four volumes. Volume 1 deals with (part 1) the radio-activity of radium, the technique of radium therapy, dosage, measurement of radium plaques, and radium teletherapy; (part 2) the biological effects of radiation, including radiosensitivity, the mode of action of radiation, the effects of radium on normal tissues and malignant tumours, tissue culture and experimental radiology, and the dangers of radium, and protection. The volume is well illustrated and referenced.

Chest Examination: The Correlation of Physical and X-Ray Findings in Diseases of the Lung, by Richard R. Trail, M.C., M.D., F.R.C.P., in its third edition (J. & A. Churchill Ltd., 12s. 6d.) contains a new chapter on miliary shadowing, and another on lung tumours. Coming from the pen of the Medical Director of Papworth and Enham-Alamein Village Settlement the revised edition of this authoritative work will receive a warm welcome.

NOTES AND PREPARATIONS

NEW PREPARATIONS

MAGSILATE chewing tablets (acetylsalicylic acid 5 grains, magnesium trisilicate $1\frac{1}{2}$ grains, magnesium hydroxide $1\frac{1}{2}$ grains, sugar and flavouring q.s.) are prepared with a special protective film to ensure the stability of the active ingredient. It is claimed that incorporation of the antacids renders the preparation suitable for those unable to tolerate ordinary acetylsalicylic acid, and that the thorough mastication by chewing ensures the minimum of irritation to the gastric mucosa with maximum absorption (The Westminster Laboratories Ltd., Chalcot Road, London, N.W.1).

MANDAMINE brand of hexydaline (methenamine mandelate) combines the two established

urinary antiseptics, methenamine and mandelic acid, in one distinct chemical compound. It is stated to be non-cumulative in action and free from toxic effects. Its use is indicated particularly in cases of pyelitis of pregnancy, in urinary infections in children, and for prolonged therapy in obstinate and inoperable cases. The manufacturers are Menley & James Ltd., 119-123 Coldharbour Lane, London, S.E.5, who issue the product in bottles of 60 and 500 tablets of 0.25 gm.

NEODRENAL brand isopropyl adrenaline (Savory & Moore) is a stable sympathomimetic amine related to adrenaline, prepared for oral administration in the treatment of bronchial asthma. It is stated to exert a strong broncho-

problem is infinitely more complex and this book interprets the well-known phenomena of malaria in the light of the new knowledge. There are two introductory chapters, the first dealing with symptomatology and the second with the malaria parasites; the latter being written by Dr. R. H. Black. The main chapters are devoted to each organ in turn and are divided into four parts: (1) clinical evidence of dysfunction including biochemical changes; (2) macroscopic and microscopic appearances; (3) pathogenesis (now interpreted largely in terms of anoxia); and (4) a most useful recapitulation. The subject of immunity is not discussed in much detail and a few organs (e.g. placenta, lungs) are omitted; in all other respects the book provides a complete and masterly review of the subject.

Streptomycin und Tuberkulose. EDITED BY G. FANCONI and W. LÖFFLER. Basle: Benno Schwabbe & Co., 1948. Pp. 357. Illustrated. Price Sw. frs. 30.

THIS comprehensive monograph is a record of Swiss work on streptomycin in tuberculosis. Whilst predominantly clinical, there are interesting chapters on the experimental aspects of the subject, and a particularly useful concluding section on the post-mortem findings in cases of tuberculous meningitis treated with streptomycin. Workers in this country will be especially interested in the three chapters devoted to a comparison of streptomycin, para-aminosalicylic acid and a sulphone derivative. Clinically the Swiss results are comparable to those obtained in Great Britain, but it is interesting to note that the Swiss workers have found streptomycin a useful adjunct in Monaldi drainage. This is a work which will repay careful attention by all who are concerned with the use of streptomycin in tuberculosis.

Petticoat Surgeon. BY BERTHA VAN HOSEN. London: Peter Davies, 1948. Pp. 334. Price 12s. 6d.

DR. VAN HOSEN was born on a Michigan farm in 1863 and entered College in 1880. She chose medicine at a time when women doctors were rarities, laughed at and discouraged. She fought her way through to the position of one of America's leading surgeons, and paid for herself at all stages of her career. For this grand old lady every year of her life has been a joyous adventure. She writes impetuously, conversationally, pouring out her life story as if she were recounting it to a friend; but so interesting has been that life, so clear is her memory of incidents that happened many years ago, and so exact her command of English, her choice of the irreplaceable phrase, that she has produced a far better story than she could have con-

structed with the most careful arrangement at revision. This is the finest "autobiography" of Medicine; one that every doctor should read and every woman doctor should possess.

Management in Obstetrics. BY A. N. CLAYE, M.D., F.R.C.S., F.R.C.O.G. London: Oxford University Press, 1948. Pp. vi and 156. Figures 17. Price 12s. 6d.

THIS is a most useful book both for student and for practitioner. It is small and concise and as the author explains, tends to be dogmatic; it loses nothing of its value by this, as it emphasizes sound principles of management, with which most obstetricians will, in the main, agree. The quotations which appear at the beginning of many of the chapters are apt and pleasing; if in future editions suitable quotations can be found for the remaining chapters, this most enjoyable book will be made still more pleasurable.

A Pocket Gynaecology. BY S. G. CLAYTON M.D., M.S., F.R.C.S., M.R.C.O.G. London: J. & A. Churchill Ltd., 1948. Pp. vii and 109. Figures 18. Price 7s. 6d.

By strict economy of words the author has condensed the gynaecological knowledge required for qualifying examinations in medicine into a genuine pocket book. A comprehensive orthodox factual summary, it does not neglect theory. It will make excellent revision reading for those already prepared by clinical instruction and the use of a normal textbook.

Medicine and Science in Postage Stamps. BY W. J. BISHOP, F.L.A., and N. M. MATHESON, F.R.C.S. London: Harvey & Blythe Ltd. (Distributors: H. K. Lewis & Co., Ltd.), 1948. Pp. 82. Illustrated. Price 7s. 6d.

THIS fascinating little book, which is claimed to be the first to be published on the subject, will appeal to all philatelists, whether medical or non-medical. Attention has been devoted to the historical aspects rather than to the philatelic details which are already available in standard stamp catalogues. The book is a striking commentary on the English conservatism where stamps are concerned. Except for Sir Wilfrid Grenfell, who is depicted on a Newfoundland stamp issued in 1941, none of the famous figures in British medicine has been commemorated in stamps. Even Florence Nightingale has had to depend upon Belgium and Costa Rica for such commemoration. The book is freely illustrated, but it is to be hoped that in future editions reference to the plates will be incorporated in the text.

THE PRACTITIONER

Edited by

SIR HENEAGE OGILVIE

K.B.E., D.M., M.Ch., F.R.C.S.

WILLIAM A. R. THOMSON, M.D.

W. N. MANN, M.D., F.R.C.P.

ROBERT M. STECHER, M.D., F.A.C.P.



July—December 1948

THE PRACTITIONER
5 BENTINCK STREET, LONDON, W.1

1948

All Rights Reserved

dilatory action in conjunction with a diminished vasopressor effect. Neodrenal is administered sublingually or by "oral" inhalation. For the former method tablets of 0.02 gm., in tubes of 25 or bottles of 250, are available, and for the latter a 1 per cent. spray solution in bottles of 15 and 100 c.cm. A "neodrenal" all-glass spray, complete with filler, is obtainable (Savory & Moore Ltd., 60-61 Welbeck Street, London, W.1). *Price List of Medical Products*, giving the names of products, indications for use, dosage, packings and prices, can be obtained on application.

NEW APPARATUS

THE BELCLERE AMPLIFIED STETHOSCOPE comprises a three valve amplifier which fits in the waistcoat pocket (5" by 2½" by 1" thick in moulded case; three-stage 10 m.m. valves with frequency range of 50 to 3000 cycles per second and maximum amplification of 80 decibels); chest-piece, containing piezo crystal microphone; head-piece—standard stethoscope type with magnetic earpiece attached; and batteries (John Bell & Croyden, 50-52 Wigmore Street, London, W.1, price £25 4s. complete).

ROYAL MEDICAL BENEVOLENT FUND CHRISTMAS GIFTS

THE President of the Royal Medical Benevolent Fund, Lord Webb-Johnson, P.R.C.S., in his Christmas Gifts Fund Appeal letter writes:

"I appeal once more to members of the medical profession to help those who are dependent on others for extra comforts . . . I hope that subscribers to the Fund will send donations to provide a little extra cheer at Christmas time, and I earnestly beg those who are not subscribers, not only to send Christmas Gifts but to become regular supporters of the Fund. A special effort to obtain new subscriptions is urgently necessary because certain medical bodies such as the Panel Committees, which used to make generous contributions, have gone out of existence with the National Health Service Act . . ."

Donations and subscriptions, marked "Christmas Gifts", should be sent to the Secretary, Royal Medical Benevolent Fund, 1 Balliol House, Manor Fields, Putney, London, S.W.15.

KING EDWARD VII HOSPITAL FOR OFFICERS

HER MAJESTY QUEEN MARY opened King Edward VII Hospital for Officers at Beaumont House, Beaumont Street, London, W.1 on October 15. The hospital has two wards of five beds and two of two beds, where nursing and maintenance will be free. There are also 17 single rooms, for which the charge will be much less than it would be elsewhere in London. Patients make their own arrangements with their physicians and surgeons. Regular and retired officers of the Royal Navy, the Army and the

R.A.F. are eligible for admission; also temporary officers of all three Services fought in the 1914-18 or 1939-45 wars, provided they become subscribers. The annual subscription is £1. Applications should be made to the house governor, Beaumont House, Beaumont Street, W.1. Sister Agnes founded this hospital in 1899 at 17 Grosvenor Crescent. Between then and 1941 over 10,000 officers were patients. The premises were badly damaged by bombs in January 1941, and the hospital had to be closed. It is now being opened as a hospital on the most modern lines.

NUFFIELD MEDICAL FELLOWSHIPS

For the past few years the Nuffield Foundation has offered a number of Nuffield Medical Fellowships each year in four subjects only: child health, industrial health, social medicine and psychiatry. In all there have been 11 applications for these fellowships, and 10 fellowships have been awarded. At a recent meeting the trustees decided to widen the scope of the scheme to include all fields of medicine whilst still giving special consideration to applications for additional training in the four subjects originally included. Further particulars can be obtained from the Secretary, the Nuffield Foundation, 12 and 13 Mecklenburgh Square, London, W.C.1.

PUBLICATIONS

The Rh Blood Groups and their Clinical Effect, by P. L. Mollison, A. E. Mourant and R. L. Race (H.M. Stationery Office, 1s. 6d.), issued by the Medical Research Council (Memo. No. 19) deals with the Rh blood groups, their classification and uses, their clinical significance and tests for sensitization. This work is an important addition to the literature on this subject.

The B.D.H. Guide to the B.P. 1948.—A new edition of this useful guide, the purpose of which is to direct attention to the preparations which differ in composition or strength from the corresponding preparations described in the B.P. 1932 or its Agenda, has recently been issued by the British Drug Houses Ltd, Graham Street, London, N.1, and a limited number is available for distribution.

Binding Cases for Volume 160 (January—June 1948) in green cloth with gilt lettering are now available, price 4s. post free, from the Publishing Department, *The Practitioner*, 5 Bentinck Street, London, W.1. Subscribers in Liverpool and district may like to send their copies for binding to the Sir Robert Jones Memorial Workshops, 74 Upper Parliament Street, Liverpool 8.

The contents of the December issue, which will include a symposium on "Winter Ailments", will be found on page LXXIII at the end of the advertisement section.

	PAGE
FERGUSON, T.: Some industrial aspects of rheumatism	170
FITZWILLIAMS, D. C. L.: Old gentleman's hernia	120
FLUKER, J. L.: Critical survey of the present position in the treatment of the more common specific fevers	186
GARROD, L. P.: Current therapeutics. VIII.—Surgical antiseptics	130
GAVEY, C. J.: Vitamin E in angina pectoris and coronary thrombosis	NQ 345
GOADBY, H.: Care of the elderly bronchitic patient	446
GRAHAM, S.: Child's diet in winter	454
GRAY, A.: Treatment of vaginitis	NQ 428
GREENE, R.: Treatment of obesity	NQ 510
HADDOW, A.: Teroprotein in treatment of cancer	NQ 509
HARLEY, D.: Advances in the treatment of allergy	305
—: Bronchitic asthma	NQ 509
HARRISON, M. SPENCER, and DIX, M. R.: Management of deafness	469
HAWKING, F.: Choice of sulphonamides	RC 219
HELLIER, F. F.: Advances in dermatology	290
—: Hyperæsthesia in urticaria	NQ 509
HELLIJAS, C. S., and TOVELL, R. M.: Newer inhalational anæsthetics	361
HODGSON, G.: Cheilitis exfoliativa	NQ 344
HORDER, LORD: Signs and symptoms of impending death	73
HUNTER, R. B.: Cough mixtures	449
JANEWAY, C. A.: Current therapeutics. X.—Clinical use of gamma globulin	333
KENDALL, D.: Parpanit and neurotrasentin in Parkinson's disease	NQ 146
KERSLEY, G. D.: Present status of gold therapy in rheumatoid arthritis	158
KING, A.: Treatment of syphilis in pregnancy	NQ 66
KINMONT, P. D. C.: Treatment of vitiligo	NQ 428
KORKIS, F. BOYES: Pharyngeal abscesses in young children	199
LAW, W. A.: Surgical treatment of rheumatoid arthritis	163
LEAK, W. N.: Care of the dying	80
—: Drugs in country practice	406
LEAR, G. S.: Embalming and cremating	94
LEAROYD, C. G.: A glass of beer	123
MACARTHUR, Sir W.: "Sweating Sickness"	NQ 223
MACGREGOR, M.: Nocturnal enuresis	RC 504
MCNEE, J. W.: Advances in the treatment of diseases of the liver	284
MAEGRAITH, B.: Advances in tropical medicine	325
MAGEE, A. V.: Pruritus in industry	409
MANN, I.: Advances in ophthalmology	317
MANN, W. N.: Alkali therapy in peptic ulcer	NQ 64
MILLAR, T. McW.: Anæsthesia in minor surgery	372
MUSHIN, W. W.: Intravenous anæsthesia	353
NASH, D. F. ELLISON: Clicking jaw	RC 61
NAYAR, P. T. K.: Treatment of halitosis	NQ 429
NEALE, A. V.: Advances in pædiatrics	261
NIXON, W. C. W.: Habitual abortion	NQ 65
NORRISH, R. E.: Residual dilatation of the upper urinary tract following pregnancy	47
OGILVIE, Sir HENEAGE: Then and now	1
PAGE, I. H.: Arterial transfusion	479
PATERSON, A. SPENCER: Stammering	RC 341
PONIEDEL, C.: Instructive case of dermatitis artefacta	487
PORRITT, A. E.: New Zealand state medical service	29
RAWLINGS, K. O.: Use and abuse of aspirin	RC 423
RINK, E. H.: Choice of anæsthetic in elderly patients	390
RUSBY N. LLOYD: Treatment of acute infections of the respiratory tract	437
RUSHTON, M. A.: Advances in the treatment of oral and dental diseases	321
RYLE, J. A.: Modern concept of social medicine	5

GENERAL INDEX

TO VOLUME 161

SYMPOSIA

	PAGE
Symposium on social medicine	1-38
— on thanatology in general practice	73-107
— on the problem of rheumatism	153-185
— on advances in treatment	233-332
— on anæsthetics in general practice	353-395
— on winter ailments	437-468

INDEX TO NAMES OF AUTHORS

Abbreviations: *abs*—Abstract; *NQ*—Note and Query; *RC*—Revision Corner

AIRD, I.: Advances in surgery		247
ALSTEAD, S., and CHAMBERS, J. WILSON: Current therapeutics. XII.—Newer barbiturates		490
BANKS, A. L.: National Health Service Act		11
—: Euthanasia		101
—: Health Act and the Services	NQ	345
BARBER H.: Act of dying		76
BARBER, H. W.: Recurrent boils	NQ	344
BARNES, J.: "Safe period" and birth control	NQ	65
BATEMAN, G.: Advances in otology		311
BAUER, L. H., and BAUER, W. W.: Social medicine in the United States of America		21
BETT, W. R.: Practice of medicine eighty years ago		34
BISHOP, P. M. F.: Current therapeutics. IX.—Oestrogens		211
—: Control of excessive uterine bleeding	NQ	427
Black, D. A. K.: Idiopathic steatorrhœa	RC	593
BOIAM, R. M.: Care of the skin in winter		461
BOOME, E. J.: Stammering in childhood	NQ	428
BOWES, K.: Analgesia in labour	NQ	65
BRAMWELL, C.: Advances in cardiology		274
BRITTON, C. J. C.: Allergy to eggs	NQ	224
BUSH, J. P.: Hydramnios		113
BUTTER, A. J. M.: Current therapeutics. XI.—Modern treatment of epilepsy		417
CAPENER, N. L.: Spinal deformities in the third decade	NQ	224
CHAMBERS, J. WILSON, and ALSTEAD, S.: Current therapeutics. XII.—Newer barbiturates		490
CHRISTIE, R. V.: Subacute bacterial endocarditis	NQ	64
CLARKSON, P.: Facial injuries in road accidents		396
COHEN, H.: Advances in medicine		233
COLLINS, D. H.: Laboratory aids in the diagnosis of rheumatism		180
—: Wintrobe hæmatocrit technique	NQ	429
CONNELL, W. K.: Tobias and the doctors		411
CONYBEARE, E. T.: Vaccination against smallpox		108
—: Inoculation of infants	NQ	429
CREW, F. A. E.: Genes and sex determination	NQ	144
CRITCHLEY, M.: Advances in the treatment of nervous diseases		280
CROOKE, A. C.: Advances in endocrinology		298
—: Treatment of gynæcomastia	NQ	510
CROSS, A. G.: Conjunctivitis	RC	340
—: Solution for use with contact lenses	NQ	510
CULLINAN, E. R.: Recurrent pyrexia of uncertain origin	NQ	145
DAVIS, E. D. D.: Treatment of coryza	RC 339 NQ	509
DIX, M. R., and HARRISON, M. SPENCER: Management of deafness		469
DOCKERY, G.: Hypertrichosis (hirsuties)	RC	59
DOUTHVAITE, A. H.: Problem of rheumatism		153
DOWLING, G. B.: Chilblains and their treatment		465
EVANS, F.: Pethidine-hyoscine-trilene analgesia	NQ	225
—: Anæsthetist's bag	RC	425
EVANS, R. G.: Halitosis	RC	140

	PAGE
Anæsthesia in obstetrics, general indications for	389
—, inhalation	361, 389
—, —, in obstetrics, drugs for	386
—, intravenous	353
—, —, hazards of	358
—, —, in obstetrics, drugs for	388
—, —, in minor surgery	373
—, —, methods of	354
—, local, in country practice	408
—, premedication in, use of barbiturates	496
—, suffocation during, in facial injuries	397
Analgesia in obstetrics	385
—, local, in minor surgery	374
—, —, technique of	376
—, pethidine-hyoscine-trilene	NQ 225
—, surface	377
Analgesics, new	52
—, synthetic	54
Angina pectoris and coronary thrombosis, treatment of, vitamin E	NQ 345
—, —, treatment of, pyribenzamine	abs 67
Angiospasm, cerebral, treatment of, papaverine	abs 228
Antibiotics	133
—, new	240
Antihistamine agents in dermatology	291
—, drugs in allergic diseases	305
Antisepsis, practical	134
Antiseptics, modern	131
—, older, drawbacks of	131
—, surgical	130
Anuria, sulphathiazole, renal decapsulation for	abs 228
Aorta, coarctation of, treatment of, operative	276
Arterial disease, occlusive, treatment of, amidone (methadon)	abs 148
Arthritis, rheumatoid, etiology of	155
—, —, gold therapy of, present status	158
—, —, —, —, toxic reactions	156, 159
—, —, of extremities, treatment of, surgical	164
—, —, subcutaneous nodules in, biopsy of	185
—, —, treatment of, surgical, indications	163
Asthma, bronchitic	NQ 509
—, in children	266
—, treatment of	307
Aureomycin	abs 511
Aurocalcium (calcium aurothiomalate), in rheumatoid arthritis	159
Bank notes, dirty, and infection	NQ 429
Banting's diet	120
Barbiturates, chemical structure and names of	490, 491
—, classification of, by duration of action	492
—, contraindications and toxic effects	499, 500
—, modern	490
—, therapeutic uses of	498
—, —, —, and disadvantages of	493
—, use of in obstetrics	386
Basal narcotics	381, 497
Beer, bacteriologically safe	125
—, manufacture of	123
—, nutritional value of	124
Benadryl, topical application of	abs 431
Bilharzia research in Africa	207
Bilharziasis, hepatic, liver biopsy in	abs 149
Birth control, "safe period" and	NQ 65
Bismuth oxychloride in syphilis	203
Bladder, papilloma of, treatment of, podophyllin	abs 348
Blood, chemistry of, in rheumatism	182
—, counts, seasonal variation in	abs 147
—, diseases of, treatment of, advances in	242
—, —, picture in rheumatism	181
—, —, transfusion, arterial, technique and indications	479

	PAGE
SIMPSON, S. L.: Treatment of undescended testicles - - - -	483
SKOTTOWE, I.: Recognition and management of psychiatric disorders in the field of general medicine - - - -	39
SMITH, S.: Some medical and legal problems of death - - - -	88
STFCHER, R. M.: Heberden's nodes; the importance of osteoarthritis of the fingers to the practising physician - - - -	176
STEEL, G. C.: Analgesia and anæsthesia in obstetrics - - - -	385
THOMAS, F. W. PROSSER: Sunburn, prevention and treatment - - - -	49
—: Dirty bank notes and infection - - - -	NQ 429
THOMSON, W. A. R.: African medicine - - - -	204
TOVELL, R. M., and HELLIJAS, C. S.: Newer inhalational anæsthetics - - - -	361
WAYNE, E. J.: Current therapeutics. VII.—Newer analgesics - - - -	52
WEBER, F. PARKES: Fibrous nodules on the fingers - - - -	NQ 223
WHITFIELD, A. G. W.: Differential diagnosis of headache - - - -	142
—: Treatment of headache - - - -	RC 221
WHITTLE, C. H.: Hyperhidrosis - - - -	RC 139
WILLCOX, R. R.: Chronic œdema of the penis - - - -	NQ 146
—: Rôle of bismuth oxychloride in the treatment of syphilis - - - -	203
WILLIAMS, D. I.: Greying of the hair in women - - - -	NQ 345
WITTS, L. J.: Heredity and leukaemia - - - -	NQ 144
WYATT, J.: Advances in obstetrics and gynaecology - - - -	256
WYLIE, W. D.: Pre-anæsthetic medication - - - -	379
WYLLIE, W. G.: Care of the marasmic infant - - - -	RC 62

INDEX TO SUBJECTS

Abbreviations: *abs*—Abstract; *NQ*—Note and Query; *RC*—Revision Corner

Abdomen, operations on, in elderly, anæsthesia for - - - -	394
Abdominal conditions, acute, death in - - - -	77
Abortion, habitual - - - -	NQ 65
Abscess, peritonsillar, in young children, diagnosis and treatment of - - - -	199
—, retroperitoneal, radiological sign of - - - -	228
—, retropharyngeal, in young children, diagnosis and treatment of - - - -	199
Accidents, road, facial injuries in - - - -	396
Acne, œstrogens in - - - -	217
Acridines - - - -	131
—, as antiseptics - - - -	135
Acromegaly, treatment of - - - -	298
Adanon - - - -	56
Addison's disease, treatment of - - - -	299
Adrenal crisis, treatment of - - - -	299
Adreno-cortical hyperactivity, treatment of - - - -	298
Adreno-genital syndrome with pseudo-hermaphroditism - - - -	RC 59 RC 60
Africa, medical practice in, outlook for - - - -	209
African medicine - - - -	205
Agglutination tests in rheumatism - - - -	183
Alcohol as antiseptic - - - -	134
—, effect of on brain and body - - - -	127
—, fate of in body - - - -	126
Alkaloids, opium, derivatives of - - - -	54
Allergic diseases, bacterial infection in - - - -	308
Allergy, treatment of, advances in - - - -	305
Amblyopia, nutritional - - - -	317
Ambulance services under new Act - - - -	18
Amenorrhœa, œstrogens in - - - -	216
Amidone - - - -	56
Amœbiasis - - - -	330
— in Africa - - - -	208
A.N. 148 - - - -	56
Anæmias, treatment of, advances in - - - -	242
Anæsthesia, collapse under, treatment of - - - -	86
—, for elderly patients, choice of - - - -	390
—, general, in minor surgery - - - -	373
— in minor surgery - - - -	372
— in obstetrics - - - -	385

	PAGE
Deafness, Ménière's disease and	475
—, perceptive	475
—, prenatal influences	469
—, traumatic	476
Death, certification of	91
—, famous last words	73, 76
—, impending, signs and symptoms of	73
—, last offices	94
—, legal possession and disposal	92
—, medical and legal problems	88
—, medico-legal significance, injuries and blood stains	91
—, post-mortem changes	89
—, putrefactive changes	90
—, sudden, medical aspects of	77
—, tests for	88, 100
Dehydration in treatment of epilepsy	417
Demerol	55
Dental caries	321
— diseases, treatment of, advances in	321
— services under new Act	19
Dermatitis artefacta, case report	487
—, atebria	332
—, solar	49
Dermatology, advances in	291
—, tropical	331
Desoxycorticosterone in Addison's disease	299
Detergents, cationic	132
Diabetes mellitus, treatment of	303
Diammon	56
Diamorphine (heroin)	54
Diarrhoea, infantile, epidemic, gamma globulin in	338
Diasone in tuberculosis	236
Dicoumarol in coronary thrombosis	278
Diet, children's, in winter	454
Diffuorophosphonate (DFP) in ophthalmology	318
Digitalis in cough mixtures, contraindicated	452
Digitalization, rapid	abs 513
Dihydrodromorphinone (dilaudid) as analgesic, dosage of	54
Diphtheria carriers, treatment of, tyrothricin	abs 348
—, treatment of	194
Diplopia in facial injuries, treatment of	404
Divinyl ether anaesthesia	368
Dolantin	55
Dolophine	56
Drugs in country practice	406
Ductus arteriosus, patent, treatment of	275
Duodenum, atresia of, congenital, treatment of	265
Dying, act of	76
—, care of	80
—, —, —, in younger patient, powers of recovery	86
—, —, —, medical treatment	85
—, —, —, nursing	83
—, —, —, practitioner's rôle	81, 82
Dysentery, bacillary, treatment of	190
Dysmenorrhœa, œstrogens in	216
Dyspeptic conditions, drugs for	407
Eczema vaccinatum	109
Effusion, synovial, aspiration of, in rheumatism	184
Eggs, allergy to	NQ 224
Elbow joint, rheumatoid arthritis of, treatment of, surgical	164
Embalming	94
— in special conditions	95, 96, 97
—, technique of	95
Emergencies in country practice, drugs for	407
Emulsion bases	296
Endocarditis, subacute bacterial	NQ 64
—, —, —, treatment of	274

	PAGE
Boils, recurrent	344
Boxing and Parkinsonism	513
Breast, cancer of, treatment of	247
British anti-lewisite (BAL) in ophthalmology	318
—, —, use of	244
Bromo-aspirin (acetyl-5-bromosalicylic acid), dosage of	54
Bronchiectasis in children, treatment of	266
Bronchitis in elderly, treatment of	446
Broncho-pneumonia, in elderly	447
—, treatment of	187, 448
Calciferol in dermatology	296
Calculi, urinary, control of, sodium acid phosphate in	431
Cancer, oestrogens in	217
—, teropterin in	509
Cardia, carcinoma of, treatment of, operative	252
Cardiology, advances in	274
Cardiovascular emergencies, drugs for	407
Chagas' disease	331
Cheilitis exfoliativa	344
Chickenpox, gamma globulin in	336
Chilblains, predisposing factors	465
—, treatment of	467
Child, catarrhal, treatment of	444
Children, deafness in, etiology and treatment of	470
—, diet of, in winter	454
—, drugs for	271
—, pre-anæsthetic medication in	383
Chloromycetin	240
Choanal stenosis in infants, treatment of	266
Cholera vaccine, efficacy of	325
Chrysotherapy in rheumatoid arthritis	156, 159
Codeine as analgesic, dosage of	54
Cø-liac syndrome, treatment of	264
Cold, effect of, on skin	462
Colon, carcinoma of, treatment of, surgical	249
Coma, barbiturate, treatment of, picrotoxin	347
Complement fixation test in rheumatism	184
Congress, fourth international on tropical medicine and malaria, report on	325
Conjunctivitis, inclusion, treatment of	191
—, treatment of	RC 340
Contact lenses	318
—, solution for use with	NQ 510
Copper salts in rheumatoid arthritis	162
Coryza, treatment of	RC 339, 443, NQ 509
Cough mixtures, antispasmodics	452
—, expectorants	449
—, sedatives	451
Cremation	92
—, advantages of	98
Current therapeutics. VII.—Newer analgesics	52
—, VIII.—Surgical antiseptics	130
—, IX.—Oestrogens	211
—, X.—Clinical use of gamma globulin	333
—, XI.—Modern treatment of epilepsy	417
—, XII.—Newer barbiturates	490
Cushing's syndrome, hypertrichosis in	RC 60
—, treatment of	298
Cyclopropane anæsthesia	361
—, effect of on heart	362
Dacryocyst-rhinostomy in facial injuries	404
Deafness in adult, etiology and treatment of	473
— in childhood, etiology and treatment of	470
— in infancy, etiology of	470
— in old age	476
—, management of	469

	PAGE
Health centres under new Act	16
—, public, and social medicine	7
—, subnormal, in children	267
— visitors under new Act	18
Hearing aid, national	316
—, types of	477
Heart, disease of, congenital, treatment of, operative	275
— failure, congestive, death in	77
— in elderly bronchitic, treatment of	448
Heberden's nodes, clinical signs, symptoms and treatment of	178
—, pathogenesis of	176
Helminthic disease, chemotherapy of	329
Heparin in coronary thrombosis	278
Hepatitis, infective	284
—, —, gamma globulin in	336
Hernia, old gentleman's, treatment of	120
Hip joint, rheumatoid arthritis of, treatment of, surgical	167
Hirsuties, diagnosis and treatment of	RC 59
Home helps under new Act	19
— nursing under new Act	18
Hospitals in Africa	206
Hydramnios, acute	115
—, chronic	115
—, diagnosis and differential diagnosis	116
—, etiology of	113
—, prognosis and dangers of	117
—, treatment of	117
Hyperhidrosis, etiology and treatment of	RC 139
Hypertension, headache of, treatment of	RC 222
—, treatment of, sympathectomy	250
—, —, —, tetraethylammonium chloride	abs 431
Hypertrichosis, diagnosis and treatment of	RC 59
Hypostatic discoloration in death	90
Ileus, paralytic, treatment of	86
Infant feeding	261
—, marasmic, care of	RC 62
Infections, established treatment of	137
—, neonatal, treatment of	262
Influenza, treatment of	193
Inoculation of infants	NQ 429
—, prophylactic, for pertussis and measles	270
INSTRUMENTS AND APPLIANCES:	
Belclere amplified stethoscope	436
Dissecting forceps	516
Modified automatic blood lancet	abs 149
Philips "Pillotone" unit	516
Isonipecaïne	55
Isopropenyl vinyl ether, experiments with	370
Isotopes, radio-active, use of	243
Jaundice, hæmolytic, splenectomy in	255
Jaw, clicking, treatment of	RC 61
—, fractures of, treatment of	399, 402
—, rheumatoid arthritis of, treatment of, surgical	169
Kahn test in rheumatism	183
Kala azar	330
Keratoderma of palms and soles, œstrogens in	217
Knee joint, rheumatoid arthritis of, treatment of, surgical	166
Kyphosis, rigid, treatment of	168
Labour, analgesia in	NQ 65
Lenses, contact, solution for	510
—, tinted	abs 69
Leprosy, chemotherapy of	326
— in Africa	209
Leukæmia, heredity and	NQ 144

	PAGE
Endocrinology, advances in	298
Entomology, medical and veterinary	332
Enuresis, nocturnal	504
—, treatment of, benzedrine	69
Epanutin in epilepsy	420
Ephedrine nasal sprays, keeping properties of	513
Epilepsy in children	270
—, treatment of —	495
—, —, —, drugs for	418
—, —, —, general measures	417
Erysipelas, treatment of	190
Erythroblastosis and hydramnios	114
Euthanasia	101
—, legal position of	102
—, medical aspects of	105
—, present-day opinion	104
Exophthalmos, hormones in relation to	318
Extremities, night cramps of	69
Eye, diseases of, diagnostic puncture in	319
—, —, —, nutritional	317
—, —, —, research in	319
Face, injuries of, in road accidents, late operations on bony structures	404
—, —, —, —, primary repair	399
—, —, —, —, removal of ingrained dirt	399, 404
—, —, —, —, treatment of	397, 401
Fallot's tetralogy	277
Feet, rheumatoid arthritis of, treatment of, surgical	165
Fenestration operation for otosclerosis	314, 474
Fevers, common specific, treatment of, present position	186
Fibrositic nodules, biopsy of	185
Fibrositis, etiology of	154
—, treatment of, β -diethylaminoethyl dehydrocholate	348
Fingers, fibrous nodules on	223
—, osteoarthritis of	176
Fractures, malar, treatment of	402
Gall-bladder, diseases of, radiological diagnosis of	432
Gamma globulin, clinical use of	333
—, —, —, safety and reactions of	334
Gastrectomy, transthoracic	252
Gastro-enteritis of infants, etiology and treatment of	190, 263
—, —, —, —, oral streptomycin in	511
Genes and sex determination	144
German measles, gamma globulin in	335
Glandular fever, treatment of	192
Goitre, intratracheal, treatment of	254
—, toxic, treatment of, operative	253
Gold therapy in rheumatoid arthritis, dosage	161
—, —, —, —, preparations	159
—, —, —, —, toxic reactions	156, 159
— thioglycolanilide (Lauron) in rheumatoid arthritis	159
Gynæcology and obstetrics, advances in	256
Gynæcomastia, treatment of	510
Hæmatocrit reading in rheumatism	181
— technique, Wintrobe	429
Hæmatoma, subdural, in infants, treatment of	266
Hæmophilia, treatment of	228
Hæmoptysis in elderly bronchitics	448
Hair in women, greying of	345
Halitosis, etiology and treatment of	429
Hands and wrists, rheumatoid arthritis of, treatment of, surgical	164
Headache, differential diagnosis of	142
—, post-traumatic	222
—, treatment of	221
—, —, —, E.C. 110	67
Health Act and the Services	345

	PAGE
Health centres under new Act	16
—, public, and social medicine	7
—, subnormal, in children	267
— visitors under new Act	18
Hearing aid, national	316
—, types of	477
Heart, disease of, congenital, treatment of, operative	275
— failure, congestive, death in	77
— in elderly bronchitic, treatment of	448
Heberden's nodes, clinical signs, symptoms and treatment of	178
—, pathogenesis of	176
Helminthic disease, chemotherapy of	329
Heparin in coronary thrombosis	278
Hepatitis, infective	284
—, —, gamma globulin in	336
Hernia, old gentleman's, treatment of	120
Hip joint, rheumatoid arthritis of, treatment of, surgical	167
Hirsuties, diagnosis and treatment of	RC 59
Home helps under new Act	19
— nursing under new Act	18
Hospitals in Africa	206
Hydramnios, acute	115
—, chronic	115
—, diagnosis and differential diagnosis	116
—, etiology of	113
—, prognosis and dangers of	117
—, treatment of	117
Hyperhidrosis, etiology and treatment of	RC 139
Hypertension, headache of, treatment of	RC 222
—, treatment of, sympathectomy	250
—, —, —, tetraethylammonium chloride	abs 431
Hypertrichosis, diagnosis and treatment of	RC 59
Hypostatic discoloration in death	90
Ileus, paralytic, treatment of	86
Infant feeding	261
—, marasmic, care of	RC 62
Infections, established treatment of	137
—, neonatal, treatment of	262
Influenza, treatment of	193
Inoculation of infants	NQ 429
—, prophylactic, for pertussis and measles	270
INSTRUMENTS AND APPLIANCES:	
Belclere amplified stethoscope	436
Dissecting forceps	516
Modified automatic blood lancet	abs 149
Philips "Pillotone" unit	516
Isonipeaine	55
Isopropenyl vinyl ether, experiments with	370
Isotopes, radio-active, use of	243
Jaundice, hæmolytic, splenectomy in	255
Jaw, clicking, treatment of	RC 61
—, fractures of, treatment of	399, 402
—, rheumatoid arthritis of, treatment of, surgical	169
Kahn test in rheumatism	183
Kala azar	330
Keratoderma of palms and soles, oestrogens in	217
Knee joint, rheumatoid arthritis of, treatment of, surgical	166
Kyphosis, rigid, treatment of	168
Labour, analgesia in	NQ 65
Lenses, contact, solution for	510
—, tinted	abs 69
Leprosy, chemotherapy of	326
— in Africa	209
Leukæmia, heredity and	NQ 144

	PAGE
Limbs, rheumatoid arthritis of, treatment of, surgical - - - -	164, 165
Lip-reading, advantages of - - - -	478
Liver, cirrhosis of, cholangiolytic - - - -	289
——, diseases of, portal cirrhosis and nutritional problems in - - - -	286
——, ———, treatment of, advances in - - - -	284
——, function tests - - - -	286
——, surgery of, advances in - - - -	288
Lung, resection of - - - -	252
Lymph glands, regional, biopsy of - - - -	185
Lymphogranuloma, inguinale, treatment of - - - -	191
Malaria, chemotherapy of - - - -	328
——, immunity in - - - -	329
—— in Africa - - - -	208
Malocclusion in jaw fractures, correction of - - - -	404
Marasmus, etiology and treatment of - - - -	RC 62
Mastectomy dressing, postoperative - - - -	abs 430
Mastoid, surgery of - - - -	315
Maternity service under new Act - - - -	16
Measles, gamma globulin in - - - -	334
——, treatment of - - - -	193
Medicine, advances in - - - -	233
——, African - - - -	205
——, changing disciplines in - - - -	8
——, general, psychiatric disorders in field of - - - -	39
——, history of - - - -	2, 34
——, Smollett's views on - - - -	411
——, social, and public health - - - -	5, 7
——, ———, in United States of America - - - -	21
——, ———, ten point programme of American Medical Association - - - -	21
——, state, growth of - - - -	11, 12
——, ———, in New Zealand - - - -	29
——, then and now - - - -	1
——, tropical, advances in - - - -	325
Megacolon, treatment of, operative - - - -	249
Ménière's disease, and deafness - - - -	475
——, ———, treatment of, medical - - - -	314
——, ———, ———, surgical - - - -	313
Meningitis in children, treatment of - - - -	268
——, treatment of - - - -	196
Menopause, Heberden's nodes in relation to - - - -	178
——, oestrogens in - - - -	215, 217
Mental disorders, symptomatic - - - -	39
Merperidine - - - -	55
Methadon - - - -	56
Methylphenobarbitone in epilepsy - - - -	496
Metopon (methyl dihydromorphinone) as analgesic, dosage of - - - -	54
Miadone - - - -	56
Migraine - - - -	RC 143
——, treatment of - - - -	RC 221
Morphine, synthetic analogues of - - - -	54
Mumps, gamma globulin in - - - -	337
Murexide test for tophi in gout - - - -	184
Muscle biopsy in rheumatism - - - -	185
Music as adjunct to dental anaesthesia - - - -	abs 432
Myasthenia gravis, treatment of - - - -	280
Mycology, tropical - - - -	331
Myocisin (sodium aurothiomalate) in rheumatoid arthritis - - - -	159
Nails, brittle, cream for - - - -	abs 432
Narcotics, basal - - - -	381, 497
National Health Service Act - - - -	11
——, ———, ancillary services - - - -	18
——, ———, postgraduate courses - - - -	19
——, ———, scope of - - - -	13
Nephritis, acute, in tonsillitis and scarlet fever, treatment of - - - -	189
Nervous system, autonomic, unilateral disturbance in - - - -	NQ 66
——, diseases of, treatment of, advances in - - - -	280

						PAGE
Neuralgia, migrainous, ciliary and trigeminal, treatment of	-	-	-	-	-	RC 222
Neurosyphilis, treatment of	-	-	-	-	-	281
—, ———, penicillin	-	-	-	-	-	abs 68
Newborn, hæmorrhagic disease of, treatment of	-	-	-	-	-	263
New Zealand, state medical service in	-	-	-	-	-	28
Nitrogen, mustards, clinical uses of	-	-	-	-	-	abs 147
Nose, deformity of, in facial injuries, treatment of	-	-	-	-	-	405
—, fracture of, treatment of	-	-	-	-	-	402

NOTES AND PREPARATIONS:

British Empire Cancer Campaign, 231; British R' Danish Association against Tuberculosis, 152; C (D.E.P.), 231; Estigyn, 516; Ethiodan B.D.H., 352; 72; Polybden tablets, 516; Gastro-erteritis flying 352; "Inneraze" shoes for flat feet, 72; Internation. VII Hospital for Officers, 436; Magislate chewing tablets, 435; Magtriz tablets, 516; Mandamine brand of hexydaline, 435; NAPT prize for essay on colonial tuberculosis, 516; National Register of Orthoptists, 232; National Register of Speech Therapists, 232; Neodrenal brand isopropyl brand isopropyl-noradrenaline, 72; Nitrogen mustard hydrochloride, 436; Penicillin chewing gum A. & H., 352; Robaden, 516; method of testing the urine for sugar, 231; Steramide-Ag, 72; 3, 352; Tetrathylphosphosphate (T.E.P.P.), 231, T.S.R., 72.

<i>N</i> -propyl ethyl ether, experiments with	-	-	-	-	-	-	370
— methyl ether, experiments with	-	-	-	-	-	-	369
Nutritional diseases in tropics	-	-	-	-	-	-	331

Obesity, treatment of	-	-	-	-	-	-	NQ	510
Obstetrics, analgesia and anaesthesia in	-	-	-	-	-	-	-	385
— and gynæcology, advances in	-	-	-	-	-	-	-	256
— in country practice, drugs for emergencies in	-	-	-	-	-	-	-	408
—, new health service and	-	-	-	-	-	-	-	260
Oesophagus, atresia of, congenital, treatment of	-	-	-	-	-	-	-	265
—, —, —, —, —, operative	-	-	-	-	-	-	-	251
—, carcinoma of, treatment of, operative	-	-	-	-	-	-	-	252
Oestrogens	-	-	-	-	-	-	-	211
—, physiology of	-	-	-	-	-	-	-	212
—, routes of administration and dosage of	-	-	-	-	-	-	213,	214
—, therapeutic indications	-	-	-	-	-	-	-	215
Ophthalmic services under new Act	-	-	-	-	-	-	-	19
Ophthalmology, advances in	-	-	-	-	-	-	-	317
Ophthalmoplegia, exophthalmic, treatment of	-	-	-	-	-	-	-	303
Oral diseases, treatment of, advances in	-	-	-	-	-	-	-	321
Osteoarthritis, etiology of	-	-	-	-	-	-	-	153
Osteomyelitis, acute, in children, treatment of	-	-	-	-	-	-	-	267
Otitis media, acute, treatment of	-	-	-	-	-	-	-	315
—, secretory, diagnosis and treatment of	-	-	-	-	-	-	-	311
Otology, advances in	-	-	-	-	-	-	-	311
Otosclerosis and deafness	-	-	-	-	-	-	-	474
—, fenestration for	-	-	-	-	-	-	314,	474
Oubain per rectum	-	-	-	-	-	-	abs	512

Pædiatrics, advances in	- - - - -	-	-	-	-	-
Pain, pleural, treatment of, calcium gluconate	- - - - -	-	-	-	-	<i>abs</i> 149
—, relief of, drugs for —	- - - - -	-	-	-	-	- 406
Pancreas, cystic fibrosis of, treatment of	- - - - -	-	-	-	-	- 264
Para-aminosalicylic acid (P.A.S.) in tuberculosis	- - - - -	-	-	-	-	- 236
Parkinson's disease, treatment of, parpanit and neurotrasentin	- - - - -	-	-	-	-	NQ 146
Parodontal disease, etiology and treatment of	- - - - -	-	-	-	-	- 323
Parotid gland, lacerations of, treatment of	- - - - -	-	-	-	-	- 401
Passenger injuries in motor accidents	- - - - -	-	-	-	-	<i>abs</i> 147, 396
Penicillin and sulphathiazole in typhoid fever and brucellosis	- - - - -	-	-	-	-	- 236
—— as antiseptic	- - - - -	-	-	-	-	- 133, 136
—— in abscesses	- - - - -	-	-	-	-	- <i>abs</i> 430
—— in acute mastitis	- - - - -	-	-	-	-	- 258
—— in acute osteomyelitis	- - - - -	-	-	-	-	- 267
—— in acute otitis media	- - - - -	-	-	-	-	- 315
—— in acute salpingitis	- - - - -	-	-	-	-	- 259
—— in acute thromboangiitis	- - - - -	-	-	-	-	- <i>abs</i> 227
—— in children's diseases	- - - - -	-	-	-	-	- 271
—— in common specific fevers	- - - - -	-	-	-	-	- 186

	PAGE
Penicillin in corneal ulcers	abs 346
— in coryza	443
— in country practice	407
— in dermatology	293
— in diphtheria and diphtheria carriers	abs 346
— in neurosyphilis	281
— in pneumonia	441
— in puerperal infection	257
— in subacute bacterial endocarditis	274
— in syphilis	235
— in tracheobronchitis	444
— in Vincent's gingivitis	324
—, oral, in paediatrics	abs 226
—, rapid excretion of, measures to counter	234
— resistant strains, research on	234, 235
—, shortcomings of	233
—, table of infections which benefit by	241
Penis, œdema of, chronic	NQ 146
Peptic ulcer, treatment of, surgical	248
Peritonitis, chemotherapy in	abs 511
Pertussis, gamma globulin in	337
—, treatment of	193
Pethidine, dosage and toxic effects of	55
Phenobarbitone in epilepsy	419, 495
Phenytoin sodium in epilepsy	496
Phlebotomus fever	327
Physeptone, dosage and toxic effects	56
Plague	325
Pneumonia, lobar, treatment of	186
—, staphylococcal, treatment of	442
—, treatment of	437
—, virus, treatment of	442
Poisoning, barbiturate, diagnosis and treatment of	560
Poliomyelitis, acute anterior	240
—, —, in children	268
—, gamma globulin in	337
—, tropical	327
Polymyxin, experiments with	240
Porphyria, treatment of, folic acid	abs 148
Practitioner, The, fifty years ago	Advt. p. lxi, lxiii, lxi, lxix, lxxv, lxi
—, —, history of	i, 34
Pre-anæsthetic medication	375, 378, 496
—, —, dosage, children and adults	384
—, —, drugs for	380
Pregnancy, infra-red photography in	abs 226
—, œstrogens in	217
—, peptic ulcers and	abs 227
—, residual dilatation of upper urinary tract following	47
Prematurity, care in	261
Promin in tuberculosis	236
Prominal in epilepsy	420
Promizole in tuberculosis	236
Pruritus, industrial	409
Psittacosis, treatment of	191
Psychiatric disorders in field of general medicine, recognition and management of	39
Psychiatry, use of barbiturates in	498
Psychological treatment in children	271
Psychosomatic disorders	39
—, —, incidence of	41
—, —, treatment of	45
Pylorus, stenosis of, treatment of	265
Pyrexia, recurrent, of uncertain origin	NQ 145
Quadriceps, rupture of	abs 430
Rabies, eradication of, in wild animals	327
Radio-iodine in thyrotoxicosis	303

	PAGE
Radiotherapy, platelet counts in control of	148
Respiration, artificial, in anæsthetic overdose	360
Respiratory tract, acute infections of, treatment of	437
Re-vaccination	110

REVIEWS OF BOOKS:

Anæsthesia and analgesia, Recent advances in (Hever)	351
Anæsthetics, Textbook of (Minnitt and Gillies)	231
Apprentice, Clinical (Naish and Apley)	349
Bacterial and virus diseases (Parish)	230
Bacteriology, Practical handbook of (Mackie and McCartney)	151
—, Textbook of (Zinsser revised Smith)	515
Bones and joints, Radiology of (Brailsford)	435
Breast feeding (Naish)	230
British pharmacopœia, 1948, B.D.H. guide to	436
Cancer, Bilharzial, radiological diagnosis and treatment (Afifi)	230
Cardiology, Recent advances in (East and Bain)	151
Cardiography (Evans)	229
Cardiovascular diseases: their diagnosis and treatment (Scherf and Boyd)	151
Chest, diseases of, Practical manual of (Davidson)	230
— examination: the correlation of physical and X-ray findings in diseases of the lung (Trail)	435
—, Introduction to diseases of (Maxwell)	515
Chirology, Textbook of (Swanson)	514
Colon and rectum, Surgery of (Devine)	229
Communicable diseases, Handbook of, for the use of medical officers of schools	72
Diagnosis, Clinical, by laboratory methods (Todd and Sanford)	515
Dietetics in general practice (Cole)	151
Disciplines, Changing (Ryle)	350
Doctor, Training of	349
Eat and be healthy (Nicholls)	152
Education, Medical (Roberts)	349
Electrocardiography, Clinical (Scherf and Boyd)	231
Emergencies in medical practice (Edited by Birch)	433
Endocrine disorders, Major (Simpson)	71
Epilepsy (Edited by Hoch)	230
Exercises, Restoration, for women: embodying stand up and slim down (Rout)	71
Eye and orbit, Anatomy of (Wolff)	151
Fertility in general practice, Problems of (Jackson et al.)	514
First aid treatment, A.B.C. of (Whittingham)	232
Food and the principles of dietetics (Hutchison revised Mottram and Graham)	71
Gynæcology, Pocket (Clayton)	434
Headache and other head pain (Wolff)	514
Health, public, Textbook of (Frazer and Stallybrass)	71
Heart disease, Treatment of (Brans)	433
Hospitals, British (Ives)	232
Intestinal obstruction, Acute (Smith)	350
Laboratory methods, Clinical (Gradwohl)	435
Leprosy, Manual of (Muir)	350
Malaria and blackwater fever, Pathological processes in (Maegraith)	433
Malignant disease and its treatment by radium, Vol. 1 (Cade)	435
Mamputation, Treatment by (Fisher)	351
Medical defence, Sixty years of (Forbes)	352
— research, American past and present (Shyrook)	150
Medicine and science in postage stamps (Bishop and Matheson)	434
—, industrial, Practice of (Lloyd Davies)	150
—, Private enterprise or government in (Bauer)	70
Midwifery, Textbook of (Johnstone)	151
Nutrition, Human (Mottram)	229
Obstetrics and gynæcology, Recent advances in (Bourne and Williams)	435
—, Management in (Claye)	434
—, practical, Manual of (Brozue)	151
—, Queen Charlotte's textbook of	515
Ophthalmology, Handbook of (Neame and Williamson-Noble)	231
—, Modern trends in (Edited by Sorsby)	150
Oral and dental diseases (Stones)	70
Pharmacology (Goddum)	435
—, therapeutics and prescription writing (Bastedo)	351

	PAGE
<i>Psychiatric examination: extended history in cases of neurosis (Paterson)</i>	352
— of the school child (Hall)	71
<i>Psychiatry, Introduction to physical methods of treatment in (Sargant and Slater)</i>	151
—, Modern, in practice (Neustatter)	71
<i>Psychology, Clinical (Berg)</i>	515
<i>Radiology, diagnostic, Modern trends in (McLaren)</i>	514
<i>Radon: its technique and use (Jennings and Russ)</i>	351
<i>Remedies, modern, An index of (Mair)</i>	72
<i>Statistics, medical, Principles of (Hill)</i>	151
<i>Sterility and impaired fertility (Lane-Roberts et al.)</i>	351
<i>Streptomycin und tuberkulose (Edited by Fanconi and Löffler)</i>	434
<i>Surgeon, Petticoat (van Hoosen)</i>	434
<i>Surgery, Emergency, Part 1 (Bailey)</i>	71
—, Minor (Christopher)	71
—, — (Love)	351
<i>Surgical practice, British, Vols. 2 and 3 (Edited by Carling and Ross)</i>	433
<i>Therapy through interview (Lace)</i>	515
<i>Toxicology, Clinical (Thienes and Haley)</i>	351
<i>Treatment in general practice (Beckman)</i>	435
—, Index of (Edited by Hutchison)	231
<i>Trichomonas vaginitis and trichomoniasis (Trussell)</i>	150
<i>Tuberculosis in childhood (Price)</i>	515
— in the home, Care of (Maxwell)	231
— in young adults (Daniels et al.)	70

REVISION CORNER:

Anæsthetist's bag	425
Aspirin, use and abuse of	423
Care of the marasmic infant	62
Clicking jaw	61
Coryza, treatment of	339
Conjunctivitis	340
Enuresis, nocturnal	504
Halitosis	140
Headache, differential diagnosis of	142
—, treatment of	221
Hirsuties	59
Hyperhidrosis	139
Hypertrichosis	59
Stammering	341
Steatorrhœa, idiopathic	503
Sulphonamides, choice of	219
Rh factor, diseases due to, treatment of	262, 263
— in diseases of liver	288
—, present position of	256
Rheumatic diseases of joints, treatment of, parpanit	abs 512
— fever, treatment of, sodium salicylate	abs 225
Rheumatism, acute, industrial aspects of	175
—, chronic inflammatory, treatment of, intramuscular copper	abs 68
—, diagnosis of, bacteriological methods	183
—, —, biopsy methods	184
—, —, blood tests	180, 183
—, —, laboratory aids	180
—, —, urine analysis	182
—, etiology of	153
—, —, industrial trauma	172
—, incidence of, variations in regard to age and occupation	170
—, industrial aspects of	170
—, invalidism in, prophylaxis of	174
—, muscular, etiology of	154
—, nomenclature of	153
—, problem of	155
—, treatment of	157
—, X-ray findings	See Arthritis, rheumatoid
Rheumatoid arthritis	308
Rhinitis, allergic, treatment of	191
Rickettsia of typhus, treatment of	

	PAGE
Rigor mortis	89
Ringworm, treatment of	294
Rubella in mother and deafness in infant	469
Rutonal in epilepsy	420
"Safe period" and birth control	NQ 65
Scabies, treatment of, sea water	abs 513
Scarlet fever, treatment of	189
Schistosomiasis in Africa	208
Scrub typhus, treatment of	326
Sedatives, value of	87
Sedimentation rate, effect of anticoagulant therapy on	abs 431
—, in normal pregnancy	abs 512
—, in rheumatism	180
Shoulder joint, rheumatoid arthritis of, treatment of, surgical	165
Simmonds's disease, treatment of	298
Sinusitis, nasal, chronic, treatment of	RC 222
Skin blemishes, concealment of	abs 227
—, care of, in industry	464
—, —, —, in winter	461, 463
—, diseases of, simulating rheumatism, diagnosis by biopsy	185
—, —, —, treatment of, liquid oxygen	abs 67
—, normal, disinfection of	134
—, of newborn, care of	abs 512
Sleeping sickness in Africa	208
Smallpox, vaccination against	108
Smollett and doctors	411
Spastic conditions, treatment of, oral myanesis	abs 347
Spine, deformities of, in third decade	NQ 224
—, rheumatoid arthritis of, treatment of, surgical	168
Spondylitis, ankylosing, etiology of	154
Stammering	RC 341
—, in childhood, prognosis and treatment of	NQ 428
Status epilepticus, treatment of	421, 496
Steatorrhœa	264
—, idiopathic	RC 503
Streptomycin in Ménière's disease	475
—, in non-tuberculous infections	238
—, in tuberculosis	237
—, table of infections which benefit by	241
Stress incontinence	259
Sulphonamides	133
—, choice of	RC 219
—, in children's diseases	272
—, in common specific fevers	186
—, in country practice	407
—, in pneumonia	440
—, in tracheobronchitis	444
—, table of infections which benefit by	241
Sunburn, chronic	50
—, conditions following	50
—, prevention and treatment of	49
Surgery, advances in	247
—, minor, anæsthesia in	372
—, —, —, local analgesia in	377
"Sweating sickness"	NQ 223
Swimming pool infections	abs 226
Syphilis in pregnancy, treatment of	NQ 66
—, treatment of, rôle of bismuth oxychloride	203
Teeth, caries of	321
Tension, relief of, home hydrotherapy	abs 347
Teroplerin in treatment of cancer	NQ 509
Testicles, undescended, classification and diagnosis of	484
—, —, —, treatment of	483
—, —, —, —, hormone	485
Thanatology	73

Therapeutics, eighty years ago	-	-	-	-	-	-	-	-	-
Thiopentone anaesthesia	-	-	-	-	-	-	-	-	353,
Thiouracil in thyrotoxicosis	-	-	-	-	-	-	-	-	245, 253,
Thorax, operations on, in elderly, anaesthesia for	-	-	-	-	-	-	-	-	-
Thorium X in dermatology	-	-	-	-	-	-	-	-	-
Thrombosis, coronary, anticoagulant therapy	-	-	-	-	-	-	-	-	-
Tobias and doctors	-	-	-	-	-	-	-	-	-
Tonsillitis, treatment of	-	-	-	-	-	-	-	-	-
Tophi, murexide test for	-	-	-	-	-	-	-	-	-
Tracheobronchitis, acute, treatment of	-	-	-	-	-	-	-	-	-
Trachoma, treatment of	-	-	-	-	-	-	-	-	-
Trichlorethylene anaesthesia	-	-	-	-	-	-	-	-	-
—, effect of, on heart	-	-	-	-	-	-	-	-	-
Tridione in <i>petit mal</i>	-	-	-	-	-	-	-	-	-
Trismus in jaw fractures, treatment of	-	-	-	-	-	-	-	-	-
Trypanosomiasis	-	-	-	-	-	-	-	-	-
Tuberculosis, B.C.G. vaccination	-	-	-	-	-	-	-	-	-
— in Africa	-	-	-	-	-	-	-	-	-
—, treatment of, drugs	-	-	-	-	-	-	-	-	-
—, —, —, <i>p</i> -aminosalicylic acid	-	-	-	-	-	-	-	-	<i>abs</i>
Typhoid fever, treatment of	-	-	-	-	-	-	-	-	-
Ulcers of mouth, oestrogens in	-	-	-	-	-	-	-	-	-
—, peptic, treatment of, alkali	-	-	-	-	-	-	-	-	<i>NQ</i>
Undulant fever, treatment of	-	-	-	-	-	-	-	-	-
United States of America, social medicine in	-	-	-	-	-	-	-	-	-
Ureter, dilatation of, following pregnancy	-	-	-	-	-	-	-	-	-
—, transplantation of	-	-	-	-	-	-	-	-	-
Urinary tract infections, treatment of, sulphathalidine	-	-	-	-	-	-	-	-	<i>abs</i>
—, —, —, upper, residual dilatation of, following pregnancy	-	-	-	-	-	-	-	-	-
Urine, analysis of, in rheumatism	-	-	-	-	-	-	-	-	1
Urticaria, hyperaesthesia in	-	-	-	-	-	-	-	-	<i>NQ</i>
Uterus, excessive bleeding of	-	-	-	-	-	-	-	-	<i>NQ</i>
—, —, —, —, oestrogens in	-	-	-	-	-	-	-	-	2
Vaccination after infancy	-	-	-	-	-	-	-	-	1
— against smallpox	-	-	-	-	-	-	-	-	1
—, local reactions	-	-	-	-	-	-	-	-	1
— of infants, primary	-	-	-	-	-	-	-	-	10
—, results of	-	-	-	-	-	-	-	-	110, 11
Vaccinia, primary, typical	-	-	-	-	-	-	-	-	11
Vaginitis, atrophic, oestrogens in	-	-	-	-	-	-	-	-	21
— treatment of	-	-	-	-	-	-	-	-	<i>NQ</i>
Vaginal myoma in peptic ulcer	-	-	-	-	-	-	-	-	24
Vagina, treatment of	-	-	-	-	-	-	-	-	19
Vaginal, treatment of	-	-	-	-	-	-	-	-	19
Vincent's angina, treatment of	-	-	-	-	-	-	-	-	19
Virilism, signs of	-	-	-	-	-	-	-	-	<i>RC</i>
Viruses, neurotropic, isolation of	-	-	-	-	-	-	-	-	32
Vitamins and minerals in child's winter diet	-	-	-	-	-	-	-	-	45
Vitiligo, treatment of	-	-	-	-	-	-	-	-	<i>NQ</i>
Voluntary Euthanasia (Legalization) Bill, 1936	-	-	-	-	-	-	-	-	100
Warts, plantar, etiology and treatment of	-	-	-	-	-	-	-	-	<i>abs</i>
Wassermann test in rheumatism	-	-	-	-	-	-	-	-	183
Winter, care of skin in	-	-	-	-	-	-	-	-	461
—, children's diet in	-	-	-	-	-	-	-	-	454
Wounds, disinfection of	-	-	-	-	-	-	-	-	135
—, necrotic, débridement of	-	-	-	-	-	-	-	-	<i>abs</i>
Wrists and hands, rheumatoid arthritis of, treatment of, surgical	-	-	-	-	-	-	-	-	164
Yellow fever, control of	-	-	-	-	-	-	-	-	326
— research in Africa	-	-	-	-	-	-	-	-	207

	PAGE
Therapeutics, eighty years ago	31
Thiopentone anaesthesia	353, 37
Thiouracil in thyrotoxicosis	245, 253, 30
Thorax, operations on, in elderly, anaesthesia for	39
Thorium X in dermatology	29
Thrombosis, coronary, anticoagulant therapy	27
Tobias and doctors	41
Tonsillitis, treatment of	18
Tophi, murexide test for	11
Tracheobronchitis, acute, treatment of	4
Trachoma, treatment of	1
Trichlorethylene anaesthesia	3
—, effect of, on heart	3
Tridione in <i>petit mal</i>	4
Trismus in jaw fractures, treatment of	4
Trypanosomiasis	3
Tuberculosis, B.C.G. vaccination	3
—, in Africa	2
—, treatment of, drugs	2
—, —, —, <i>p</i> -aminosalicylic acid	abs
Typhoid fever, treatment of	1
Ulcers of mouth, oestrogens in	2
—, peptic, treatment of, alkali	NQ
Undulant fever, treatment of	1
United States of America, social medicine in	
Ureter, dilatation of, following pregnancy	
—, transplantation of	2
Urinary tract infections, treatment of, sulphathalidine	abs
—, —, —, upper, residual dilatation of, following pregnancy	3
Urine, analysis of, in rheumatism	1
Urticaria, hyperaesthesia in	NQ
Uterus, excessive bleeding of	NQ
—, —, —, —, oestrogens in	2.
Vaccination after infancy	10
—, against smallpox	10
—, local reactions	11
—, of infants, primary	10
—, results of	110, 11
Vaccinia, primary, typical	11
Vaginitis, atrophic, oestrogens in	21
—, treatment of	NQ
Vagotomy in peptic ulcer	24
Vagotomy, treatment of	19
Vagotomy, treatment of	19
Vincent's angina, treatment of	19
Virilism, signs of	RC
Viruses, neurotropic, isolation of	32
Vitamins and minerals in child's winter diet	45
Vitiligo, treatment of	NQ
Voluntary Euthanasia (Legalization) Bill, 1936	103
Warts, plantar, etiology and treatment of	abs
Wassermann test in rheumatism	183
Winter, care of skin in	461
—, children's diet in	454
Wounds, disinfection of	135
—, necrotic, débridement of	abs
Wrists and hands, rheumatoid arthritis of, treatment of, surgical	164
Yellow fever, control of	326
—, —, —, —, research in Africa	207

